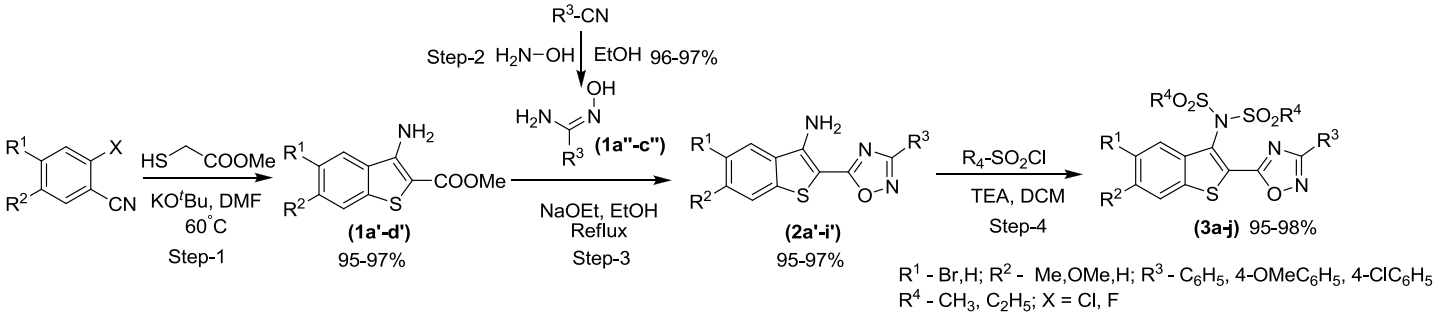
# SUPPORTING FILE

## 1. Synthesis and spectral datas of (3a – 3j) :

### Synthesis of 2-(5-Substituted-[1,2,4] oxadiazol-5-yl)-benzo[b]thiophen-3-yl bis sulfonamides




The 3-Amino-substituted benzo[b]thiophene-2-carboxylic acid methyl esters **(1a'-d')** were prepared from the reaction of the o-halonitriles and methyl 2-mercaptoacetate in the presence of potassium t-butoxide as base in N,N-dimethylformamide at $80^0$C for 3 h. In step-2 the (E)-N'-hydroxy-benzimidamide were prepared from the reaction of the nitriles and hydroxylamine in ethanol at reflux for 2h. The product from step-1 (**1a'-d'**) were treated with different (E)-N'-hydroxy-benzimidamide (**1a''-c"**) obtained from step-2 in ethanol with sodiumethoxide as base at $80^0$C to get Substituted-2-(3-substituted-1,2,4-oxadiazol-5-yl)benzo[b]thiophen-3-amine (**2a'-i'**). The compound **2a'-i'** were further treated with sulfonyl chloride in dichloromethane and triethylamine as base to get title compound 2-(5-Substituted-[1,2,4] oxadiazol-5-yl)-benzo[b]thiophen-3- yl bis sulfonamides (**3a-j**).

### 3-Amino-substituted benzo[b]thiophene-2-carboxylic acid methyl ester (1a'-d'):

To a solution of corresponding o-halobenzonitriles (1.0eq) in N,N-dimethylformamide (5v) at $0^0$C added methyl 2-mercaptoacetate (1.05eq). The mixture was stirred at $0^0$C for 30 minutes and potassium t-butoxide (1.1eq) was added. After stirring at $50^0$C for 3h, the reaction mixture was quenched with ice-water and the resulting precipitate collected by filtration and dried to get 3-Amino-substituted benzo[b]thiophene-2-carboxylic acid methyl ester (1a'-d').

### Methyl 3-aminobenzo[b]thiophene-2-carboxylate (1a'):

This compound obtained as yellow solid, yield 1.17g (96%); $^1$H NMR (DMSO-$d_6$): δ 3.79 (m, 3H, $CH_3$), 7.18 (s, 2H, $NH_2$), 7.38-7.42 (m, 2H, Ar), 7.49-7.53 (m, 1H, Ar), 7.83 (s, 1H, Ar), 8.14 (s, 1H, Ar); MS: (M+), m/z 208; Anal. Calcd. for $C_{10}H_9NO_2S$ : C, 57.95; H, 4.38; N, 6.76. Found: C, 57.88; H, 4.34; N, 6.76. Found: C, 57.82; H, 4.40; N, 6.70.

**Methyl 3-amino-5-bromobenzo[b]thiophene-2-carboxylate (1b'):**

This compound obtained as white solid, yield 1.2g (97%); $^1$H NMR (DMSO-$d_6$): δ 3.77 (m, 3H, $CH_3$), 7.19 (s, 2H, $NH_2$), 7.57 (dd, 1H, Ar), 8.07 (d, 1H, Ar), 8.14 (d, 1H, Ar); MS: (M+1), m/z 287.2; Anal. Calcd. for $C_{10}H_8BrNO_2S$ : C, 57.95; H, 4.38; N, 6.76. Found: C, 57.88; H, 4.34; N, 6.69.

**Methyl 3-amino-6-methylbenzo[b]thiophene-2-carboxylate (1c'):**

This compound obtained as white solid, yield 1.25g (95%); $^1$H NMR (DMSO-$d_6$): δ 2.39 (m, 3H, $CH_3$), 3.75 (m, 3H, $CH_3$), 7.09 (s, 2H, $NH_2$), 7.32 (d, 2H, Ar), 7.69 (s, 1H, Ar), 7.93 (s, 1H, Ar); MS: (M+1), m/z 222; Anal. Calcd. for $C_{11}H_{11}NO_2S$ : C, 59.71; H, 5.01; N, 6.33. Found: C, 59.65; H, 5.13; N, 6.37.

**Methyl 3-amino-6-methoxybenzo[b]thiophene-2-carboxylate (1d'):**

This compound obtained as white solid, yield 1.25g (97%); $^1$H NMR (DMSO-$d_6$): δ 3.78 (m, 3H, $CH_3$), 3.82 (m, 3H, $CH_3$), 7.12 (s, 2H, $NH_2$), 7.15 (s, 1H, Ar), 7.68-7.70 (m, 2H, Ar), 7.68-7.70 (m, 2H, Ar); MS: (M+1), m/z 238; Anal. Calcd. for $C_{11}H_{11}NO_3S$ : C, 55.68; H, 4.67; N, 5.90. Found: C, 55.62; H, 4.72; N, 5.85.

**General procedure for the synthesis of Substituted (E)-N'-hydroxy-benzimidamide (1a''-c''):**

To a solution of corresponding aryl nitriles (1.0eq) in ethanol (10v) added Hydroxylamine (1.5eq) and stirred at reflux for 2h. Reaction monitored by tlc, after the completion of reaction, the reaction mixture was concentrated and crystallised to get corresponding (E)-N'-hydroxy-benzimidamide.

**(E)-N'-hydroxy-benzimidamide (1a"):**

This compound obtained as white solid, yield 1.30g (97%); $^1$H NMR (DMSO-$d_6$): δ 5.80 (s, 2H, $NH_2$), 7.36-7.38 (s, 3H, Ar), 7.66-7.68 (m, 2H, Ar), 9.62 (s, 1H, OH); MS: (M+1), m/z 137.2; Anal. Calcd. for $C_7H_8N_2O$ : C, 61.75; H, 5.92; N, 20.58. Found: C, 61.69; H, 5.86; N, 20.66.

**(E)-N'-hydroxy-4-methoxybenzimidamide (1b"):**

This compound obtained as white solid, yield 1.20g (96%); $^1$H NMR (DMSO-$d_6$): δ 3.75 (s, 3H, $CH_3$), 5.69 (s, 2H, $NH_2$), 6.96 (d, 2H, Ar), 7.59 (m, 2H, Ar), 9.43 (s, 1H, OH); MS: (M+1), m/z 167; Anal. Calcd. for $C_8H_{10}N_2O_2$ : C, 57.82; H, 6.07; N, 16.86. Found: C, 57.87; H, 6.01.; N, 16.84.

**(E)-N'-hydroxy-4-chlorobenzimidamide (1c"):**

This compound obtained as white solid, yield 1.21g (97%); $^1$H NMR (DMSO-$d_6$): δ 5.85 (s, 3H, $CH_3$), 7.40-7.43 (m, 3H, Ar), 7.65-7.68 (m, 2H, Ar), 9.71(s, 1H, OH); MS: (M+1), m/z 167; Anal. Calcd. for $C_7H_7ClN_2O$ : C, 49.28; H, 4.14; N, 16.42;Found: C, 49.35; H, 4.10.; N, 16.46.

**General procedure for the synthesis of Substituted-2-(3-substituted-1,2,4-oxadiazol-5-yl)benzo[b]thiophen-3-amine (2a'-3i'):**

To a solution of 3-Amino-substituted benzo[b]thiophene-2-carboxylic acid methyl ester 1a'-d' (1.0eq) and (E)-N'-hydroxy-benzimidamide 1a"-c" (1.1eq) in ethanol, added sodium ethoxide and stirred at $80^0$C for 10h. After the completion of reaction, the reaction mixture was concentrated to remove ethanol. Then diluted with ethylacetate, washed with water, dried over $Na_2SO_4$ and evaporated under reduced pressure. The crude obtained was then purified by column to afford title compound Substituted-2-(3-substituted-1,2,4-oxadiazol-5-yl)benzo[b]thiophen-3-amine 2a'-i'.

**2-(3-phenyl-1,2,4-oxadiazol-5-yl)benzo[b]thiophen-3-amine (2a'):**

This compound obtained as white solid, yield 0.67g (95%); $^1$H NMR (DMSO-$d_6$): δ 7.44 (s, 2H, $NH_2$), 7.47-7.60 (m, 5H, Ar), 7.93 (d, 1H, Ar), 8.15 (s, 2H, Ar), 8.25-8.28 (m, 1H, Ar);

MS: (M+1), m/z 294; Anal. Calcd. for $C_{16}H_{11}N_3OS$ : C, 65.51; H, 3.78; N, 14.32; Found: C, 65.45; H, 3.71; N, 14.37.

**2-(3-(4-methoxyphenyl)-1,2,4-oxadiazol-5-yl)benzo[b]thiophen-3-amine (2b'):**

This compound obtained as yellow solid, yield 0.75g (96%); $^1$H NMR (DMSO-$d_6$): δ 3.94 (s, 3H, $CH_3$), 7.10 (s, 2H, $NH_2$), 7.43-7.57 (m, 4H, Ar), 7.94 (d, 1H, Ar), 8.09 (s, 1H, Ar), 8.26 (d, 1H, Ar); MS: (M+1), m/z 324.4; Anal. Calcd. for $C_{17}H_{13}N_3O_2S$ : C, 63.14; H, 4.05; N, 12.99; Found: C, 63.24; H, 4.16; N, 12.91.

**5-bromo-2-(3-phenyl-1,2,4-oxadiazol-5-yl)benzo[b]thiophen-3-amine (2c'):**

This compound obtained as white solid, yield 0.63g (97%); $^1$H NMR (DMSO-$d_6$): δ 7.54 (s, 2H, $NH_2$), 7.59-7.68 (m, 4H, Ar), 8.17-8.24 (m, 3H, Ar), 8.30 (s, 1H, Ar); MS: (M+1), m/z 372.4; Anal. Calcd. for $C_{16}H_{10}BrN_3OS$ : C, 51.63; H, 2.71; N, 11.29; Found: C, 51.70; H, 2.65; N, 11.36.

**5-bromo-2-(3-(4-methoxyphenyl)-1,2,4-oxadiazol-5-yl)benzo[b]thiophen-3-amine (2d'):**

This compound obtained as yellow solid, yield 0.67g (95%); $^1$H NMR (DMSO-$d_6$): δ 3.84 (s, 3H, $CH_3$), 7.10-7.13 (m, 2H, Ar), 7.49 (s, 2H, $NH_2$), 7.63-7.66 (m, 4H, Ar), 8.08-8.19 (m, 2H, Ar), 8.25 (d, 1H, Ar), 8.28 (s, 1H, Ar); MS: (M+2), m/z 404; Anal. Calcd. for $C_{17}H_{12}BrN_3O_2S$ : C, 50.76; H, 3.01; N, 10.45; Found: C, 50.68; H, 3.12; N, 10.38.

**5-bromo-2-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)benzo[b]thiophen-3-amine (2e'):**

This compound obtained as yellow solid, yield 0.67g (95%); $^1$H NMR (DMSO-$d_6$): δ 7.56 (s, 2H, $NH_2$), 7.65-7.67 (m, 3H, Ar), 8.19-8.23 (m, 3H, Ar), 8.29 (s, 1H, Ar); MS: (M+1), m/z 405; Anal. Calcd. for $C_{16}H_9BrClN_3OS$ : C, 47.25; H, 2.23; N, 10.33; Found: C, 47.19; H, 2.29; N, 10.28.

**6-methyl-2-(3-phenyl-1,2,4-oxadiazol-5-yl)benzo[b]thiophen-3-amine (2f'):**

This compound obtained as yellow solid, yield 0.67g (97%); $^1$H NMR (DMSO-$d_6$): δ 2.51 (s, 3H, $CH_3$), 7.40-7.42 (m, 1H, Ar), 7.47 (s, 2H, $NH_2$), 7.57-7.62 (m, 3H, Ar), 7.84 (d, 1H,

Ar), 8.10 (s, 1H, Ar), 8.17-8.19 (m, 2H, Ar); MS: (M+1), m/z 308.2; Anal. Calcd. for $C_{17}H_{13}N_3OS$ : C, 66.43; H, 4.26; N, 13.67; Found: C, 66.51; H, 4.28; N, 13.69.

**2-(3-(4-methoxyphenyl)-1,2,4-oxadiazol-5-yl)-6-methylbenzo[b]thiophen-3-amine (2g'):**

This compound obtained as yellow solid, yield 0.75g (97%); $^1$H NMR (DMSO-$d_6$): δ 2.51 (s, 3H, $CH_3$), 3.86 (s, 3H, $CH_3$), 7.13 (d, 2H, Ar), 7.40-7.42 (m, 1H, Ar), 7.43 (s, 2H, $NH_2$), 7.83 (d, 1H, Ar), 8.09-8.12 (m, 3H, Ar); MS: (M+1), m/z 338.2; Anal. Calcd. for $C_{18}H_{15}N_3O_2S$ : C, 64.08; H, 4.48; N, 12.45; Found: C, 64.13; H, 4.42; N, 12.53.

**2-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)-6-methylbenzo[b]thiophen-3-amine (2h'):**

This compound obtained as yellow solid, yield 0.75g (97%); $^1$H NMR (DMSO-$d_6$): δ 2.49 (s, 3H, $CH_3$), 7.39 (d, 1H, Ar), 7.46 (s, 2H, $NH_2$), 7.62-7.65 (m, 2H, Ar), 7.81 (d, 1H, Ar), 8.08 (s, 1H, Ar), 8.16-8.19 (m, 2H, Ar); MS: (M+1), m/z 342; Anal. Calcd. for $C_{17}H_{12}ClN_3OS$ : C, 59.73; H, 3.54; N, 12.2; Found: 59.68; H, 3.48; N, 12.24.

**6-methoxy-2-(3-(4-methoxyphenyl)-1,2,4-oxadiazol-5-yl)benzo[b]thiophen-3-amine (2i'):**

This compound obtained as yellow solid, yield 0.71g (95%); $^1$H NMR (DMSO-$d_6$): δ 3.86 (s, 6H, $CH_3$), 7.13 (d, 2H, Ar), 7.14-7.21 (m, 1H, Ar), 7.43 (s, 2H, $NH_2$), 7.83 (d, 1H, Ar), 7.88 (d, 1H, Ar), 8.10-8.13 (m, 2H, Ar); MS: (M+1), m/z 354; Anal. Calcd. for $C_{18}H_{15}N_3O_3S$ : C, 61.18; H, 4.28; N, 11.89; Found: C, 61.25; H, 4.36; N, 11.78.

**General procedure for the synthesis of 2-(5-Substituted-[1,2,4] oxadiazol-5-yl)-benzo[b]thiophen-3- yl bis sulfonamides (3a-j):**

To the cooled solution of Substituted-2-(3-substituted-1,2,4-oxadiazol-5-yl)benzo[b]thiophen-3-amine 2a'-i' (1.0eq) in dichloromethane (5v), added dropwise sulfonylchloride (2.5eq). Then stirred at room temperature for overnight. After the completion of the reaction, the reaction mixture was given water and brine wash. Organic layer was then separated, dried over sodium sulphate, concentrated and purified by column to afford the title comound 2-(5-Substituted-[1,2,4] oxadiazol-5-yl)-benzo[b]thiophen-3- yl bis sulfonamides 3a-j.

**N-(methylsulfonyl)-N-(2-(3-phenyl-1,2,4-oxadiazol-5-yl)benzo[b]thiophen-3-yl)methane sulfonamide (3a):**

This compound obtained as white solid, yield 0.149g (97%); Mp: 206-209$^0$C; IR (KBr, $cm^{-1}$): 1354 ($SO_2$); $^1$H NMR ($CDCl_3$): δ 3.63 (s, 6H, $CH_3$), 7.51-7.59 (m, 3H, Ar), 7.60-7.61 (m, 2H, Ar), 7.94-7.98 (s, 2H, Ar), 8.16 (s, 1H, Ar); $^{13}$C NMR ($CDCl_3$): δ 44.35, 123.16, 123.42, 126.26, 126.68, 126.85, 127.54, 127.65, 128.11, 129.06, 131.63, 136.86, 138.34, 169.09, 169.74 ; MS: (M+), m/z 450.4; Anal. Calcd. for $C_{18}H_{15}N_3O_5S_3$ : C, 48.09; H, 3.36; N, 9.35; Found: C, 48.15; H, 3.45; N, 9.41.

**N-(ethylsulfonyl)-N-(2-(3-phenyl-1,2,4-oxadiazol-5-yl)benzo[b]thiophen-3-yl)ethane sulfonamide (3b):**

This compound obtained as yellow solid, yield 0.15g (96%); Mp: 214-215$^0$C; IR (KBr, $cm^{-1}$): 1340 ($SO_2$); $^1$H NMR ($CDCl_3$): δ 1.49 (t, 6H, $CH_3$), 3.82-3.88 (m, 2H, $CH_2$), 3.91-3.98 (m, 2H, $CH_2$), 7.52-7.62 (m, 5H, Ar), 7.93-7.95 (m, 1H, Ar), 8.00-8.03 (m, 1H, Ar), 8.17-8.20 (m, 2H, Ar); $^{13}$C NMR ($CDCl_3$): δ 7.55, 52.07, 123.26, 123.63, 126.45, 126.75, 127.66, 127.96, 128.00, 129.04, 131.59, 137.10, 138.29, 169.00, 169.84; MS: (M+), m/z 478; Anal. Calcd. for $C_{20}H_{19}N_3O_5S_3$ : C, 50.30; H, 4.01; N, 8.80; Found: C, 50.37; H, 4.12; N, 8.88.

**N-(5-bromo-2-(3-phenyl-1,2,4-oxadiazol-5-yl)benzo[b]thiophen-3-yl)-N-(methylsulfonyl) methanesulfonamide (3c):**

This compound obtained as white solid, yield 0.135g (95%); Mp: 210-213$^0$C; IR (KBr, $cm^{-1}$): 1351($SO_2$); $^1$H NMR ($CDCl_3$): δ 3.62 (s, 6H, $CH_3$), 7.52-7.58 (m, 4H, Ar), 7.69-7.72 (m, 1H, Ar), 7.80-7.83 (m, 1H, Ar), 8.11-8.15 (m, 1H, Ar), 8.17 (d, 2H, Ar); $^{13}$C NMR ($CDCl_3$): δ 44.30, 122.58, 123.41, 124.20, 125.21, 125.94, 126.08, 127.13, 127.42, 127.53, 127.63, 129.24, 130.41, 131.71, 132.06, 135.68, 139.44, 169.11, 169.33; MS: (M+), m/z 530.4; Anal. Calcd. for $C_{18}H_{14}BrN_3O_5S_3$ : C, 40.91; H, 2.67; N, 7.95; Found: C, 40.97; H, 2.62; N, 7.86.

**N-(5-bromo-2-(3-(4-methoxyphenyl)-1,2,4-oxadiazol-5-yl)benzo[b]thiophen-3-yl)-N-(methyl sulfonyl)methanesulfonamide (3d):**

This compound obtained as yellow solid, yield 0.145g (96%); Mp: 218-219$^0$C; IR (KBr, $cm^{-1}$): 1354($SO_2$); $^1$H NMR (DMSO-$d_6$): δ 3.62 (s, 6H, $CH_3$), 3.85 (s, 3H, $CH_3$), 7.16 (d, 2H, Ar), 7.76-7.79 (m, 1H, Ar), 7.96 (d, 2H, Ar), 8.08 (d, 1H, Ar), 8.52 (d, 2H, Ar), 8.64 (s, 1H, Ar); $^{13}$C NMR (DMSO-$d_6$): δ 44.30, 55.93, 115.35, 118.27, 122.52, 126.28, 126.40, 129.37, 134.12,

140.03, 158.23, 162.46, 167.90, 170.29; MS: (M+), m/z 560; Anal. Calcd. for $C_{19}H_{16}BrN_3O_6S_3$ : C, 40.86; H, 2.89; N, 7.52; Found: C, 40.79; H, 2.80; N, 7.58.

**N-(5-bromo-2-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)benzo[b]thiophen-3-yl)-N-(methyl sulfonyl)methanesulfonamide (3e):**

This compound obtained as yellow solid, yield 0.144g (95%); Mp: 214-216$^0$C; IR (KBr, cm$^{-1}$): 1352($SO_2$); $^1$H NMR ($CD_3OD$): δ 3.53(s, 6H, $CH_3$), 7.62-7.64 (m, 2H, Ar), 7.64 (d, 1H, Ar), 7.81 (d, 1H, Ar), 8.00 (d, 1H, Ar), 8.10-8.12 (m, 2H, Ar), 8.38 (d, 1H, Ar), 8.66 (s, 1H, Ar); $^{13}$C NMR ($CD_3OD$): δ 46.95, 122.89, 124.07, 124.70, 125.85, 128.55, 129.65, 133.20, 137.68, 140.33, 157.96, 167.83, 170.06; MS: (M+), m/z 565; Anal. Calcd. for $C_{18}H_{13}BrN_3O_5S_3$ : C, 38.41; H, 2.33; N, 7.47; Found: C, 38.49; H, 2.40; N, 7.52.

**N-(2-(3-(4-methoxyphenyl)-1,2,4-oxadiazol-5-yl)benzo[b]thiophen-3-yl)-N-(methylsulfonyl) methanesulfonamide (3f):**

This compound obtained as yellow solid, yield 0.160g (97%); Mp: 208-209$^0$C; IR (KBr, cm$^{-1}$): 1349($SO_2$); $^1$H NMR ($CD_3OD$): δ 3.33(s, 6H, $CH_3$), 3.90 (s, 3H, $CH_3$), 7.08-7.12 (m, 2H, Ar), 7.46-7.49 (m, 1H, Ar), 7.53-7.57 (m, 1H, Ar), 7.89-7.92 (m, 2H, Ar), 8.00-8.06 (m, 3H, Ar); $^{13}$C NMR ($CDCl_3$): δ 40.52, 55.38, 114.16, 119.47, 122.60, 124.60, 124.38, 127.67, 129.06, 136.83, 139.43, 156.19, 161.82, 167.73, 172.32; MS: (M+), m/z 480; Anal. Calcd. for $C_{19}H_{17}N_3O_6S_3$ : C, 47.59; H, 3.57; N, 8.76; Found: C, 47.67; H, 3.63; N, 8.82.

**N-(6-methyl-2-(3-phenyl-1,2,4-oxadiazol-5-yl)benzo[b]thiophen-3-yl)-N-(methyl sulfonyl) methanesulfonamide (3g):**

This compound obtained as reddish orange solid, yield 0.145g (96%); Mp: 213-215$^0$C; IR (KBr, cm$^{-1}$): 1353($SO_2$); $^1$H NMR ($CDCl_3$): δ 2.53 (s, 3H, $CH_3$), 3.69 (s, 6H, $CH_3$), 7.26-7.36 (m, 1H, Ar), 7.41-7.51 (m, 3H, Ar), 7.53-7.56 (m, 1H, Ar), 7.75-7.81 (m, 1H, Ar), 7.81-7.84 (m, 1H, Ar), 8.15-8.18 (m, 2H, Ar); $^{13}$C NMR ($CDCl_3$): δ 21.80, 44.36, 122.53, 123.06, 126.27, 126.79, 127.05, 127.63, 129.04, 130.16, 131.59, 135.80, 137.00, 137.14, 169.03, 169.83; MS: (M+), m/z 464; Anal. Calcd. for $C_{19}H_{17}N_3O_5S_3$ : C, 47.59; H, 3.57; N, 8.76; Found: C, 47.64; H, 3.50; N, 8.85.

**N-(2-(3-(4-methoxyphenyl)-1,2,4-oxadiazol-5-yl)-6-methylbenzo[b]thiophen-3-yl)-N-(methyl sulfonyl)methanesulfonamide (3h):**

This compound obtained as yellow solid, yield 0.156g (97%); Mp: 219-220$^0$C; IR (KBr, cm$^{-1}$): 1346($SO_2$); $^1$H NMR ($CDCl_3$): δ 2.56 (s, 3H, $CH_3$), 3.63 (s, 6H, $CH_3$), 3.90 (s, 3H, $CH_3$), 7.02-7.05 (m, 2H, Ar), 7.40-7.43 (m, 1H, Ar), 7.70 (s, 1H, Ar), 7.82 (d, 1H, Ar), 8.09-8.12 (m, 2H, Ar); $^{13}$C NMR ($CDCl_3$): δ 21.29, 44.36, 55.42, 114.44, 118.69, 122.50, 123.04, 126.90, 129.27, 130.09, 135.76, 136.94, 137.16, 162.22, 168.71, 169.50; MS: (M+), m/z 494; Anal. Calcd. for $C_{20}H_{19}N_3O_6S_3$ : C, 48.67; H, 3.88; N, 8.51; Found: C, 48.58; H, 3.80; N, 8.41.

**N-(2-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)-6-methylbenzo[b]thiophen-3-yl)-N-(methyl sulfonyl)methanesulfonamide (3i):**

This compound obtained as white solid, yield 0.155g (96%); Mp: 215-216$^0$C; IR (KBr, cm$^{-1}$): 1355($SO_2$); $^1$H NMR ($CDCl_3$): δ 2.57 (s, 3H, $CH_3$), 3.63 (s, 6H, $CH_3$), 7.27-7.40 (m, 1H, Ar), 7.43 (d, 2H, Ar), 7.52 (d, 1H, Ar), 7.71(s, 1H, Ar), 7.83 (d, 1H, Ar), 8.11 (d, 2H, Ar); $^{13}$C NMR ($CDCl_3$): δ 44.33, 122.56, 123.07, 126.90, 128.93, 129.41, 130.26, 137.07, 168.59, 169.50; MS: (M+), m/z 498; Anal. Calcd. for $C_{19}H_{16}ClN_3O_5S_3$ : C, 45.82; H, 3.24; N, 8.44; Found: C, 45.76; H, 3.18; N, 8.35.

**N-(2-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)-6-methylbenzo[b]thiophen-3-yl)-N-(methyl sulfonyl)methanesulfonamide (3j):**

This compound obtained as yellow solid, yield 0.155g (98%); Mp: 218-220$^0$C; IR (KBr, cm$^{-1}$): 1351($SO_2$); $^1$H NMR ($CDCl_3$): δ 3.64 (s, 6H, $CH_3$), 3.91 (s, 3H, $CH_3$), 3.94 (s, 3H, $CH_3$), 7.03-7.06 (m, 2H, Ar), 7.23-7.28 (m, 2H, Ar), 7.33 (d, 1H, Ar), 7.81(d, 1H, Ar), 8.10-8.12 (m, 2H, Ar); $^{13}$C NMR ($CDCl_3$): δ29.71, 44.39, 55.44, 104.34, 114.46, 118.69, 118.97, 124.21, 126.72, 127.83, 129.28, 130.97, 138.16, 159.18, 162.24, 168.72, 169.47; MS: (M+), m/z 510; Anal. Calcd. for $C_{20}H_{19}N_3O_7S_3$ : C, 47.14; H, 3.76; N, 8.25; Found: C, 47.25; H, 3.81; N, 8.32.

**Spectral datas:**

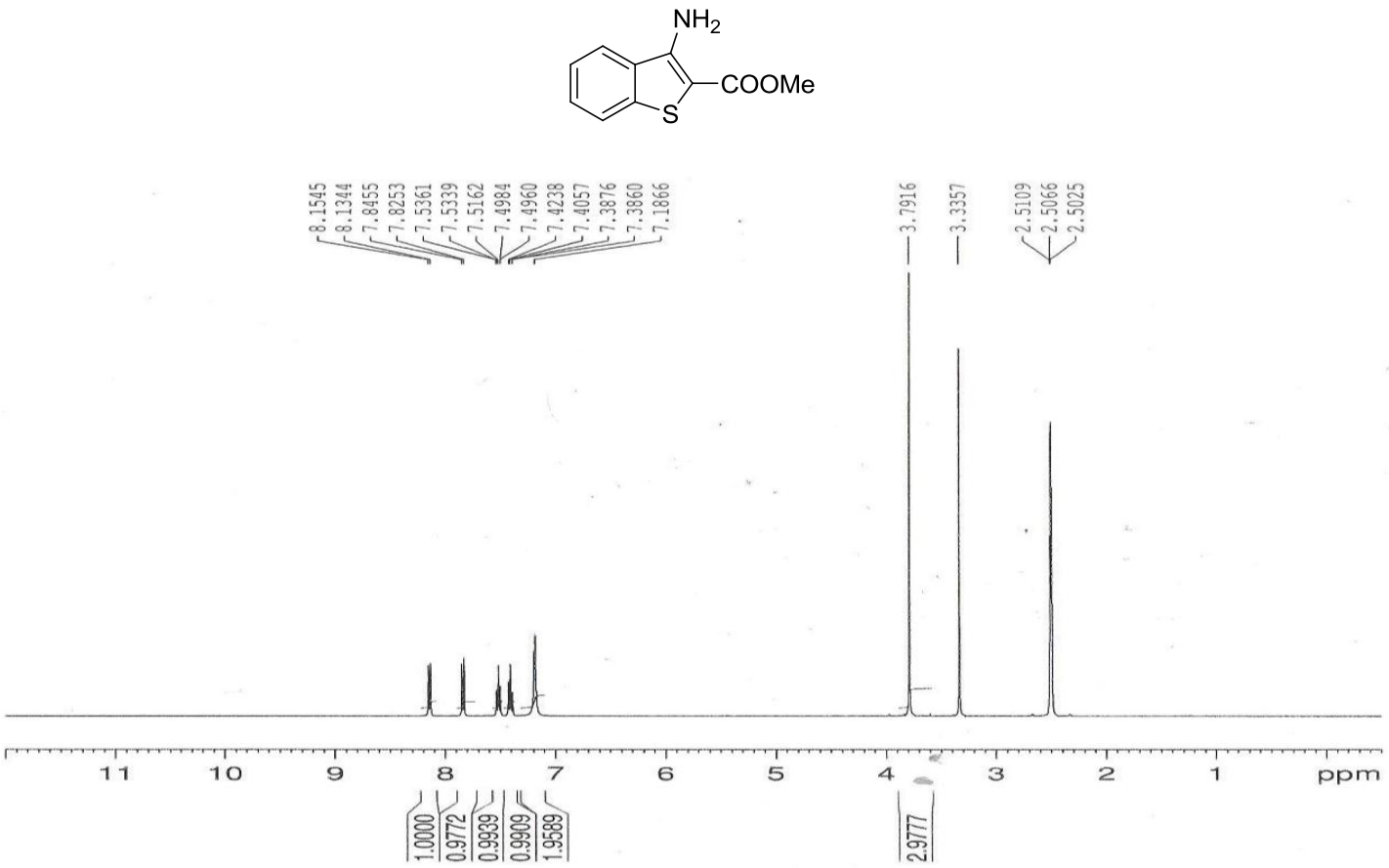



**Figure 1: 1H NMR of compound 1a' in DMSO-$d_6$**

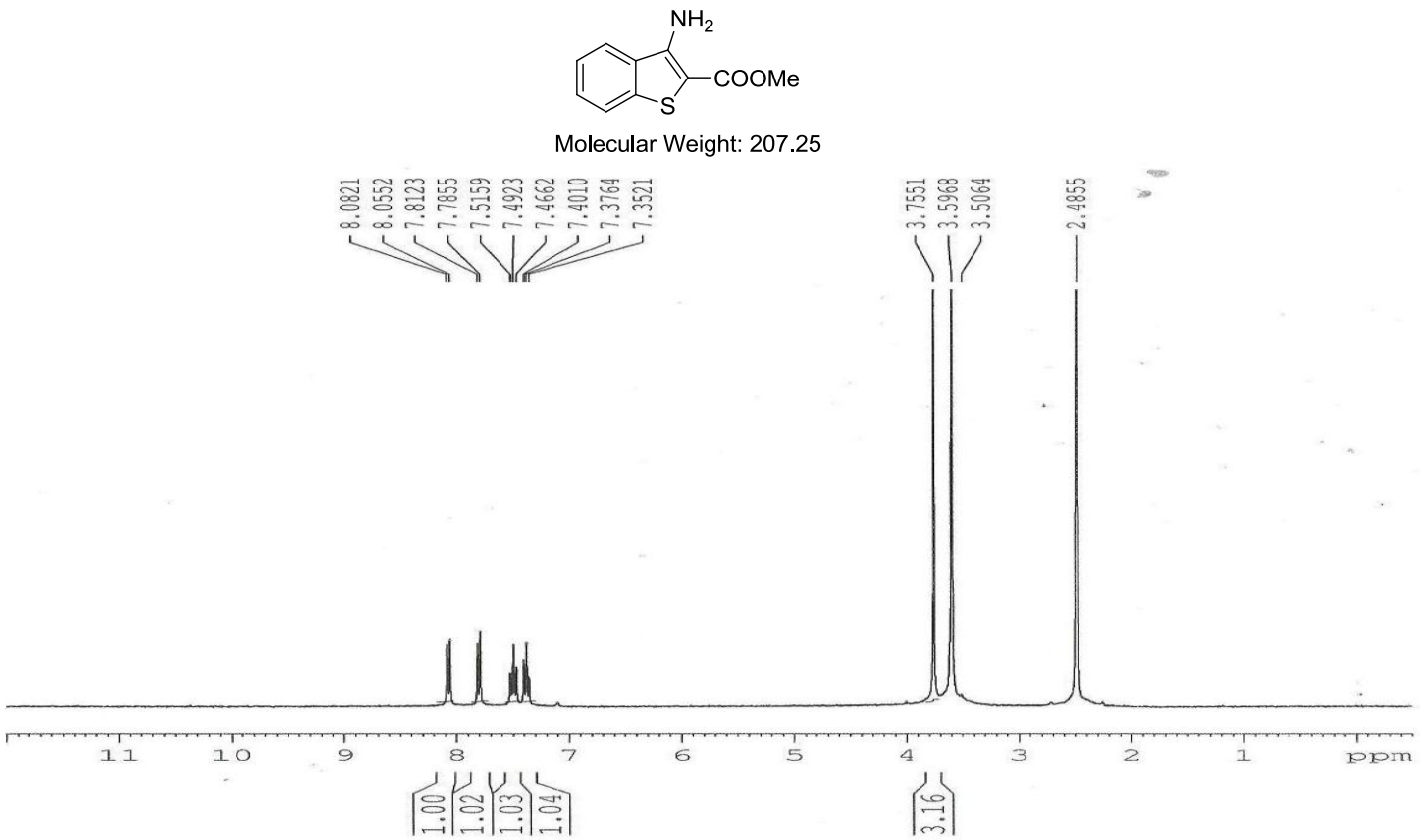
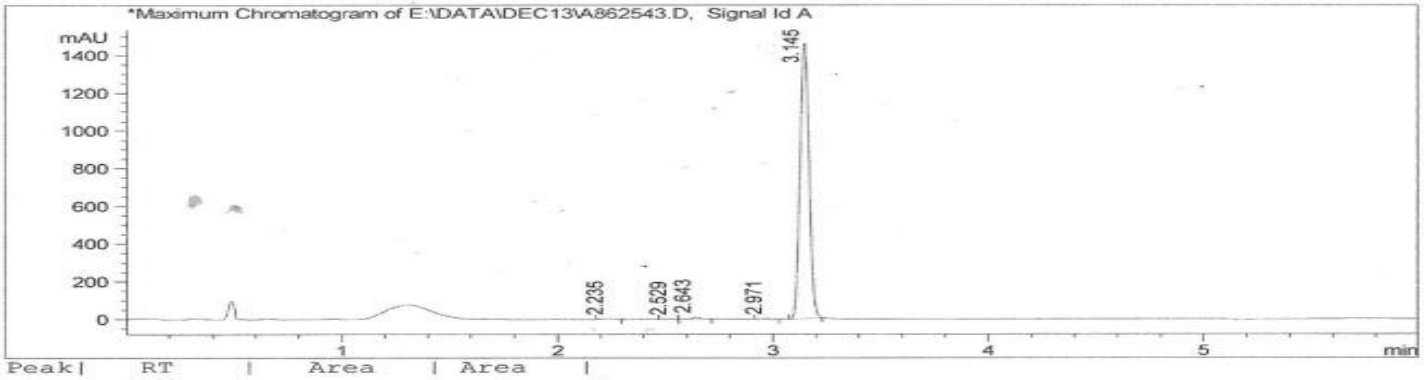



**Figure 2: 1H NMR of compound 1a' in DMSO-$d_6$ with $D_2O$-Exchange**

Method info :A-0.1%HCOOH;B-ACN Flow: 1.5ml/min,
Column-Atlantis dC18 (50X4.6mm-5µm, ) postive mode & Negative mode

| TIME (MIN) | : | 0--3.0 | 3.0--4.0 | 4.0--4.5 | 4.5-6.0 |
|---|---|---|---|---|---|
| %B | | 5-95 | 95 | 95-5 | 5 |




| Peak No | RT min | Area | Area % |
|---|---|---|---|
| 1 | 2.235 | 1.030e+001 | 0.234 |
| 2 | 2.529 | 2.819e+000 | 0.064 |
| 3 | 2.643 | 3.319e+001 | 0.755 |
| 4 | 2.971 | 1.409e+001 | 0.320 |
| 5 | 3.145 | 4.337e+003 | 98.626 |

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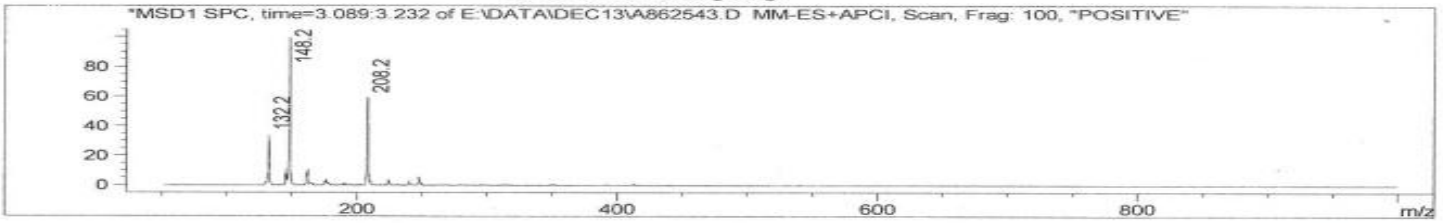
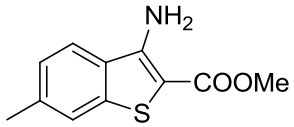



**Figure 3: LC-MS of compound 1a'**




Molecular Weight: 221.28

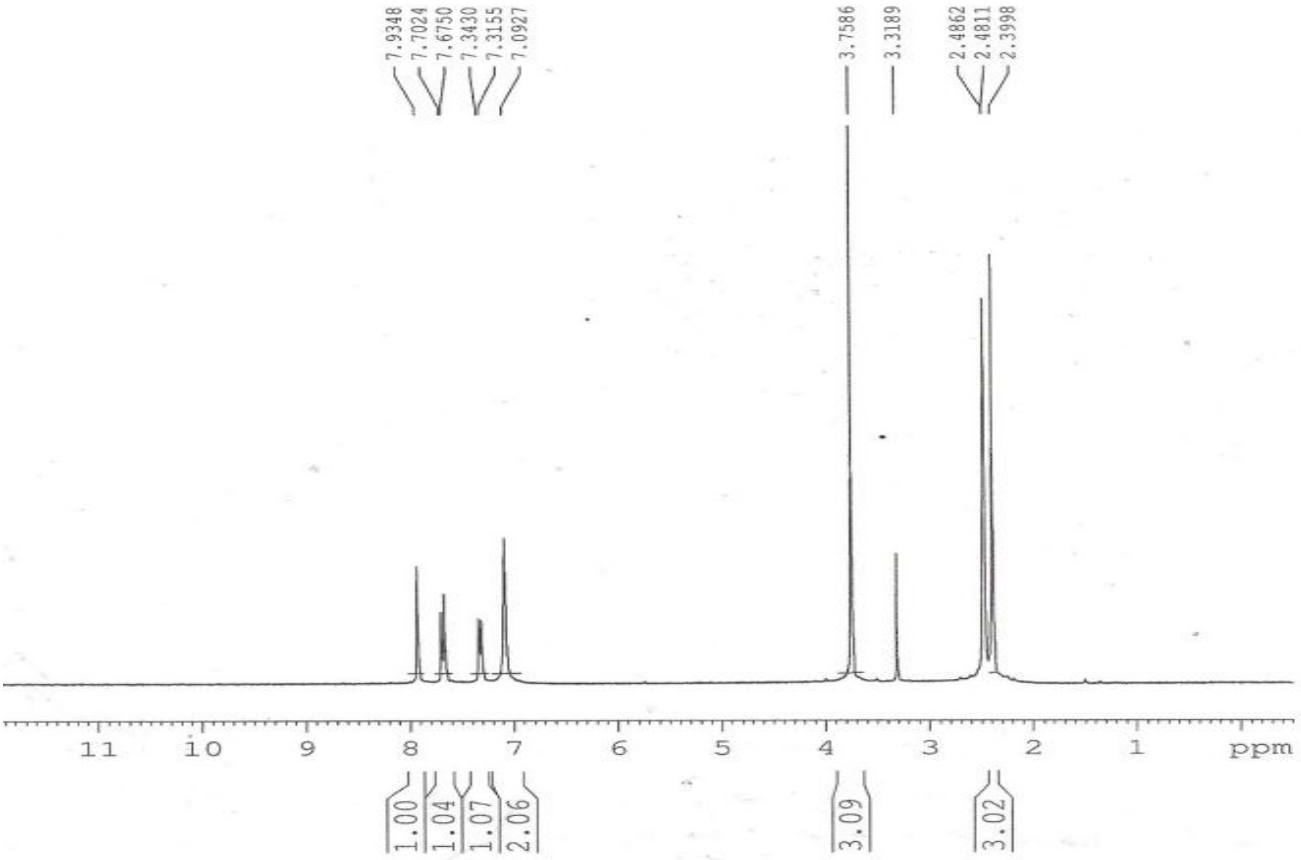
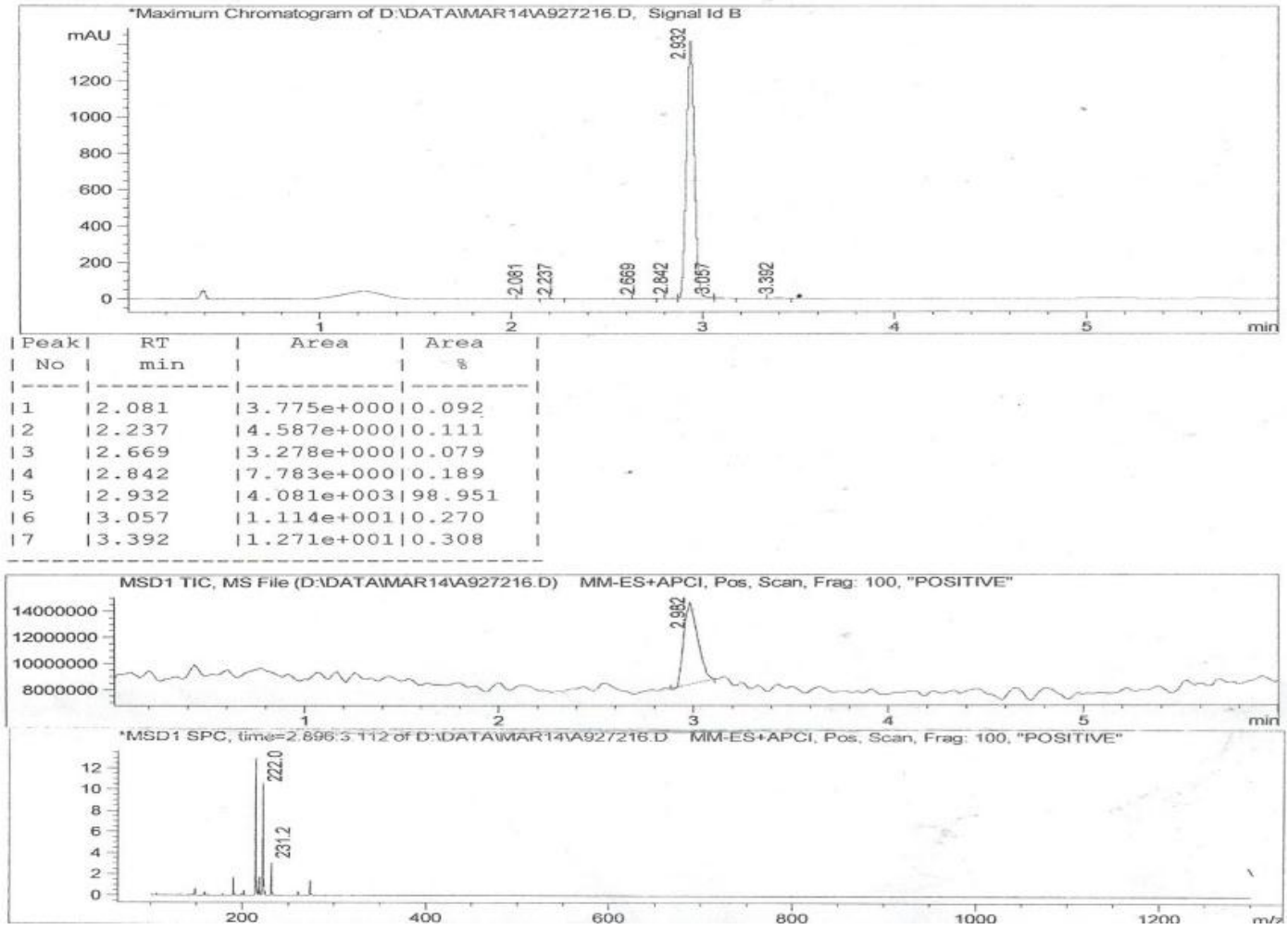



**Figure 4: 1H NMR of compound 1c' in DMSO-$d_6$**

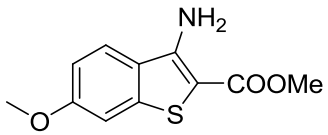
```
Method info   :A-0.1%FORMIC ACID IN WATER ;B-ACETONITRILE   Flow = 1.5ML/MIN
               Column-zorbax XDBC18 (50X4.6mm-5µm )
               Time (min.): 0--2.5 2.5--4.0    4.0--4.5   4.5--6.0
                % B :         5-95       95        95-5          5
```




| Peak No | RT min | Area | Area % |
|---|---|---|---|
| 1 | 2.081 | 3.775e+000 | 0.092 |
| 2 | 2.237 | 4.587e+000 | 0.111 |
| 3 | 2.669 | 3.278e+000 | 0.079 |
| 4 | 2.842 | 7.783e+000 | 0.189 |
| 5 | 2.932 | 4.081e+003 | 98.951 |
| 6 | 3.057 | 1.114e+001 | 0.270 |
| 7 | 3.392 | 1.271e+001 | 0.308 |




**Figure 5: LC-MS of compound 1c'**




Molecular Weight: 237.27

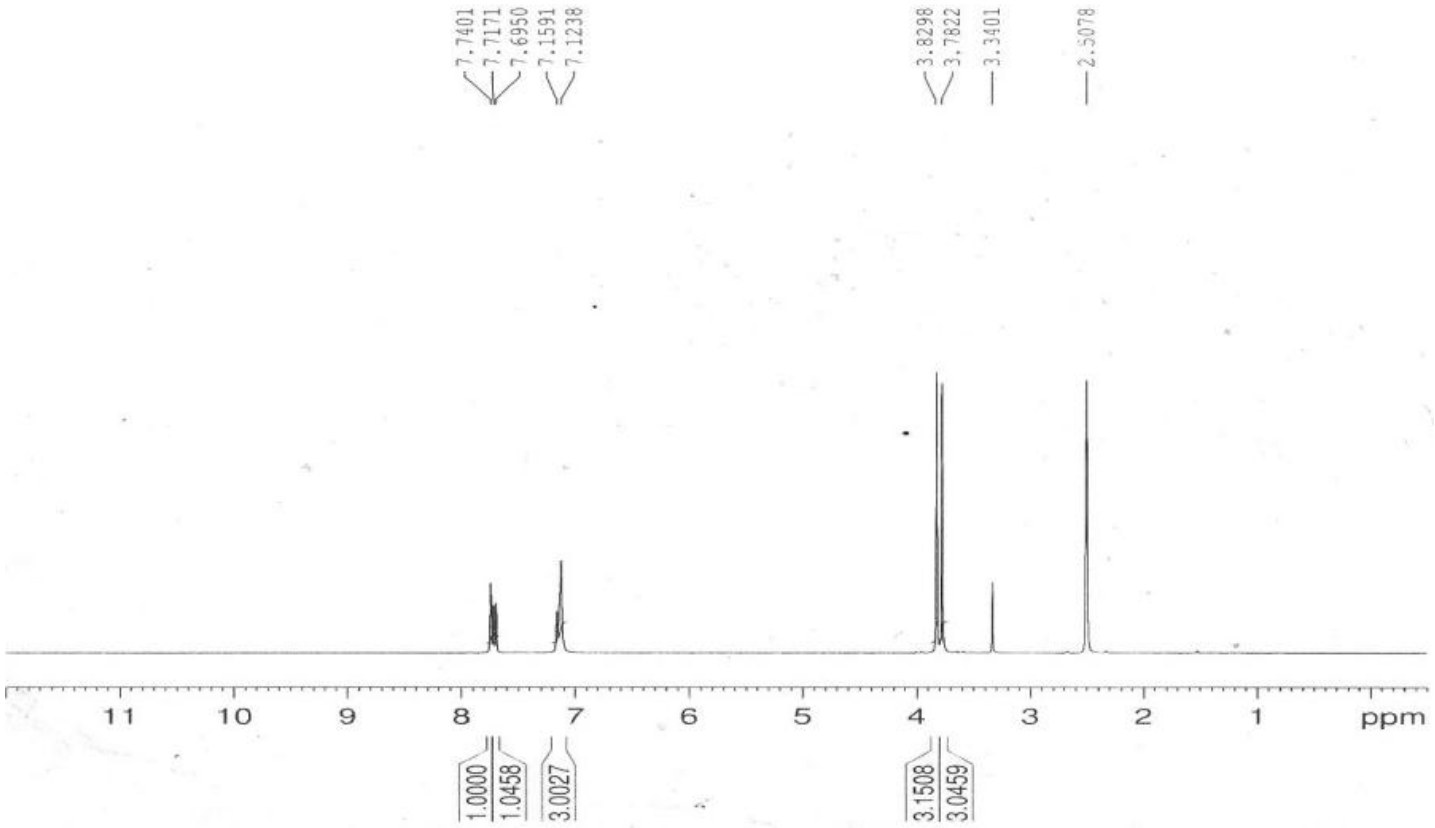
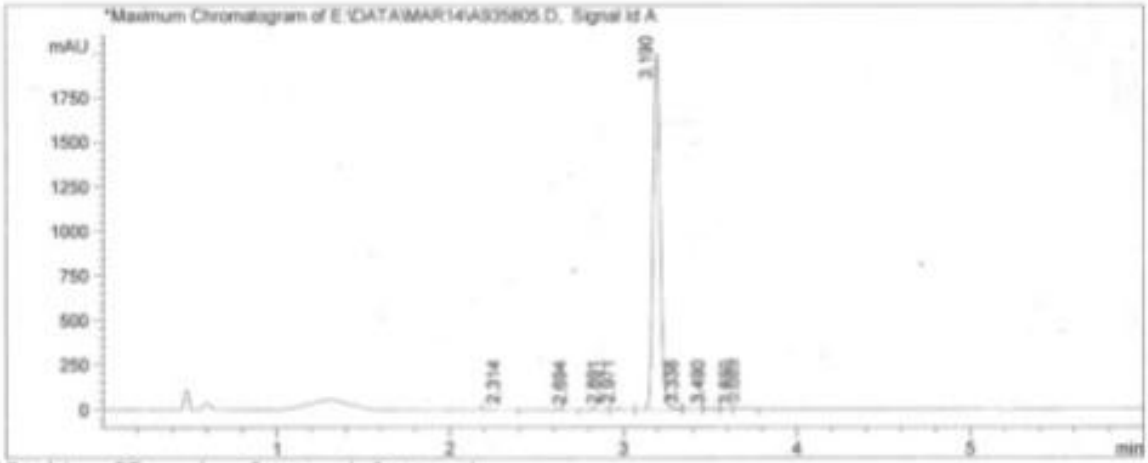
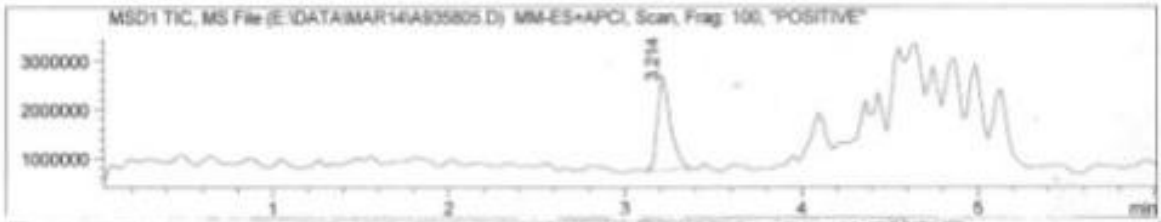



**Figure 6: 1H NMR of compound 1d' in DMSO-$d_6$**

```
Method info  :A-0.1%HCOOH;B-ACN  Flow: 1.5ml/min,
              Column-Atlantis dC18 (50X4.6mm-5µm, )  positive mode & Negative mode
              TIME (MIN)  :  0--3.0     3.0--4.0     4.0--4.5     4.5-6.0
                    %B         5-95        95         95-5          5
```




| Peak No | RT min | Area | Area % |
|---|---|---|---|
| 1 | 2.314 | 7.241e+000 | 0.127 |
| 2 | 2.694 | 1.254e+000 | 0.022 |
| 3 | 2.891 | 3.721e+000 | 0.065 |
| 4 | 2.971 | 1.146e+001 | 0.202 |
| 5 | 3.190 | 5.624e+003 | 98.953 |
| 6 | 3.338 | 9.366e+000 | 0.165 |
| 7 | 3.490 | 4.861e+000 | 0.086 |
| 8 | 3.650 | 2.311e+000 | 0.041 |
| 9 | 3.689 | 1.928e+001 | 0.339 |



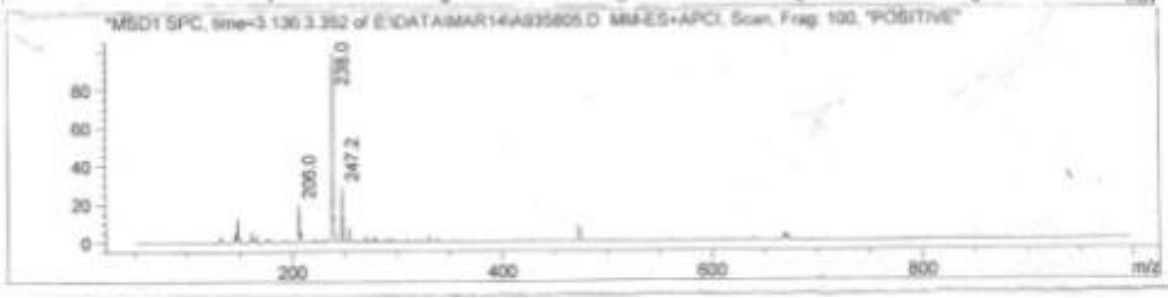
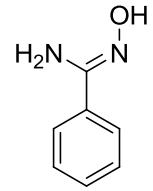




**Figure 7: LC-MS of compound 1d'**




Molecular Weight: 136.15

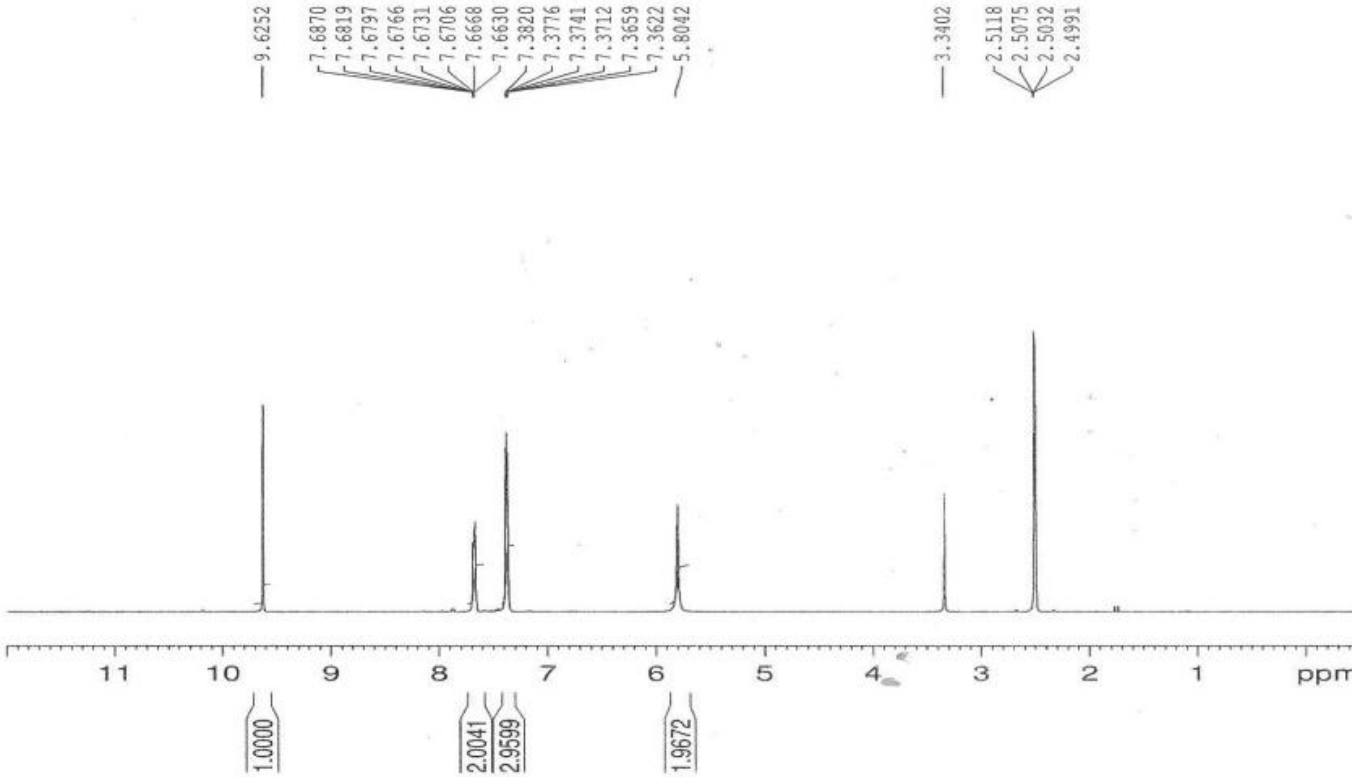
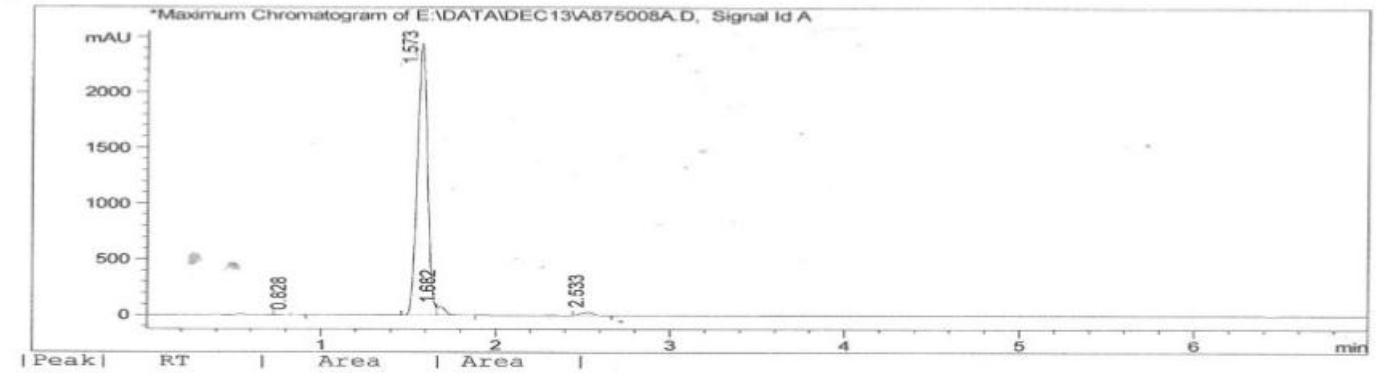
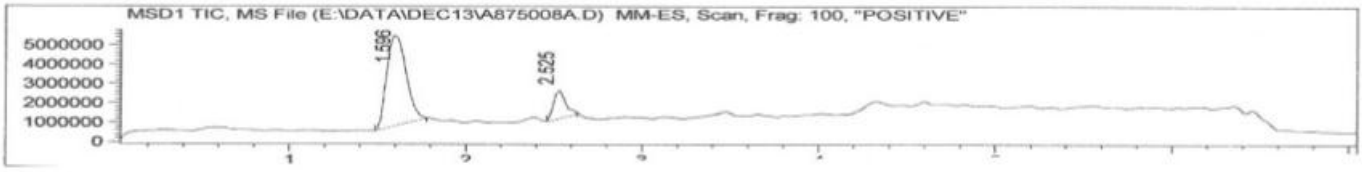



**Figure 8: 1H NMR of compound 1a" in DMSO-$d_6$**

Method info :A-10mM Ammonium acetate in water;B-Acetonitrile Flow: 1.2ml/min,
Column-ZOXBAX XDB C18 (50X4.6mm-5µm, ) positive& negative
TIME (MIN) : 0--3.0 3.0--5.0 5.0--5.5 5.5-7.0
%B 10-95 95 95-10 10




| Peak No | RT min | Area | Area % |
|---|---|---|---|
| 1 | 0.828 | 1.996e+001 | 0.192 |
| 2 | 1.573 | 9.971e+003 | 96.156 |
| 3 | 1.682 | 2.327e+002 | 2.244 |
| 4 | 2.533 | 1.460e+002 | 1.408 |

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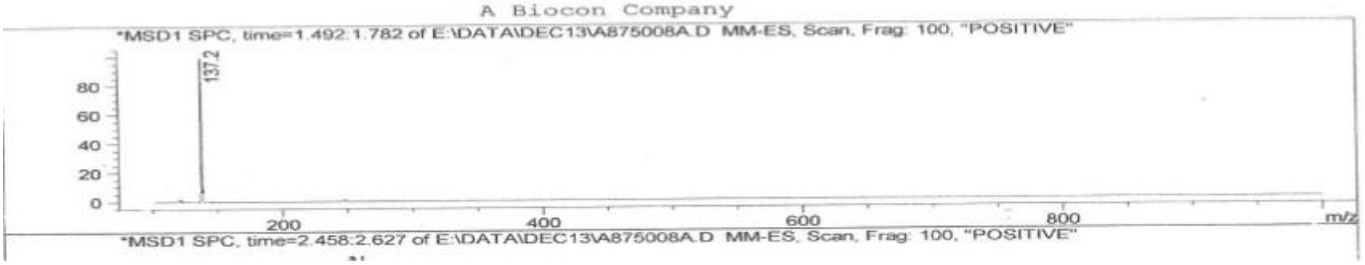



**Figure 9: LC-MS of compound 1a"**

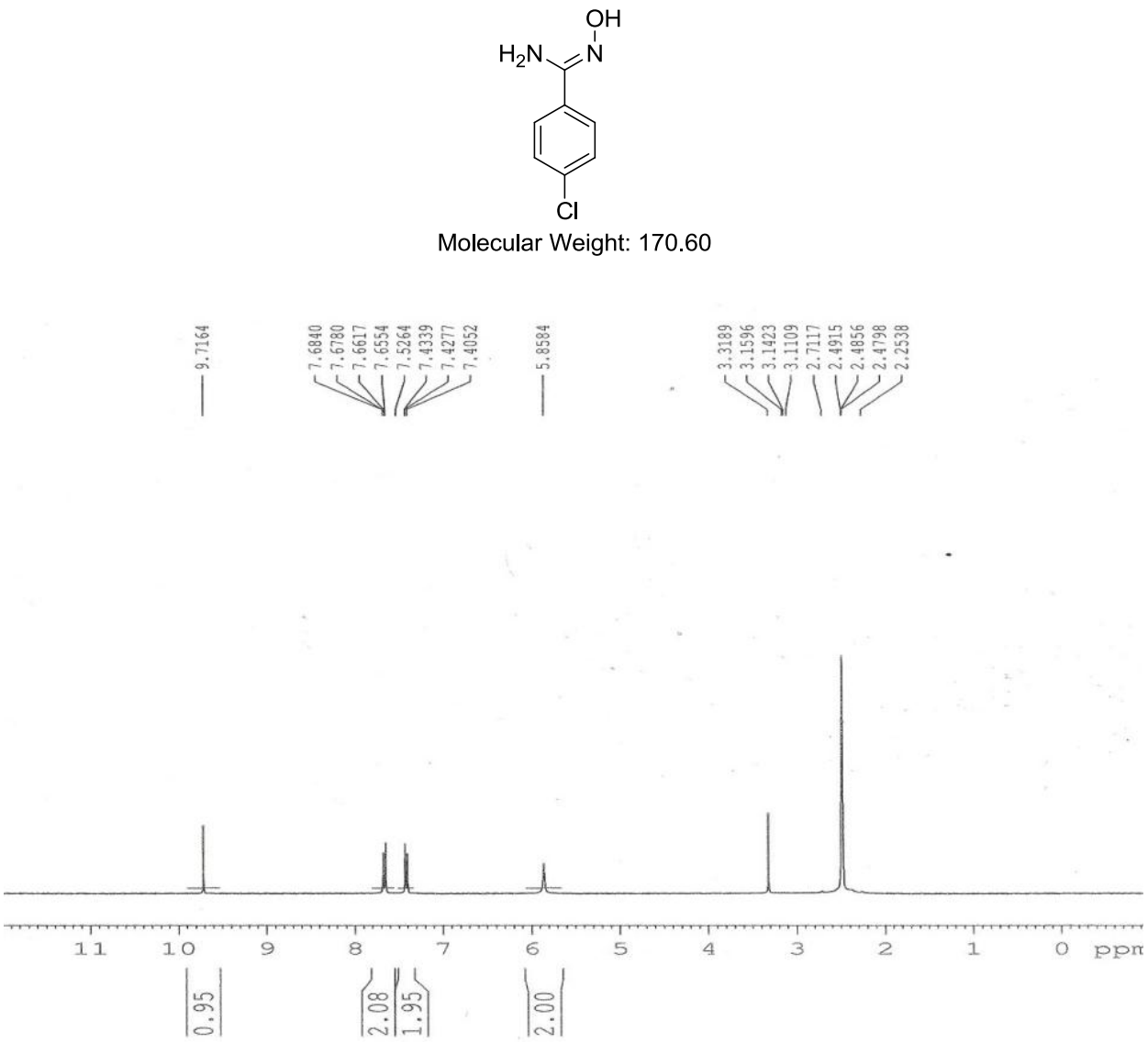
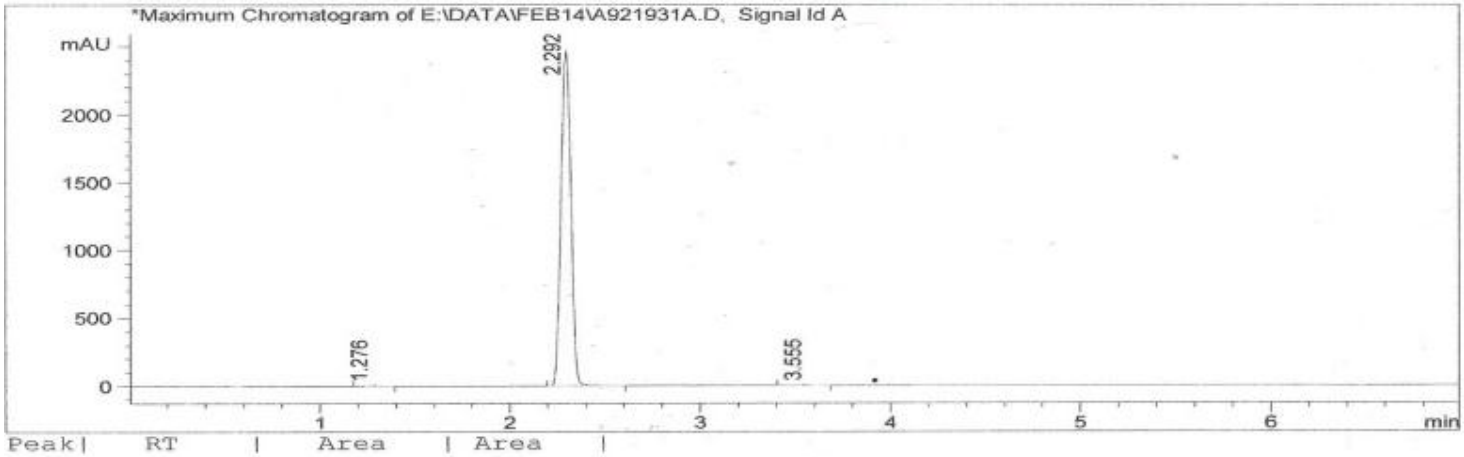
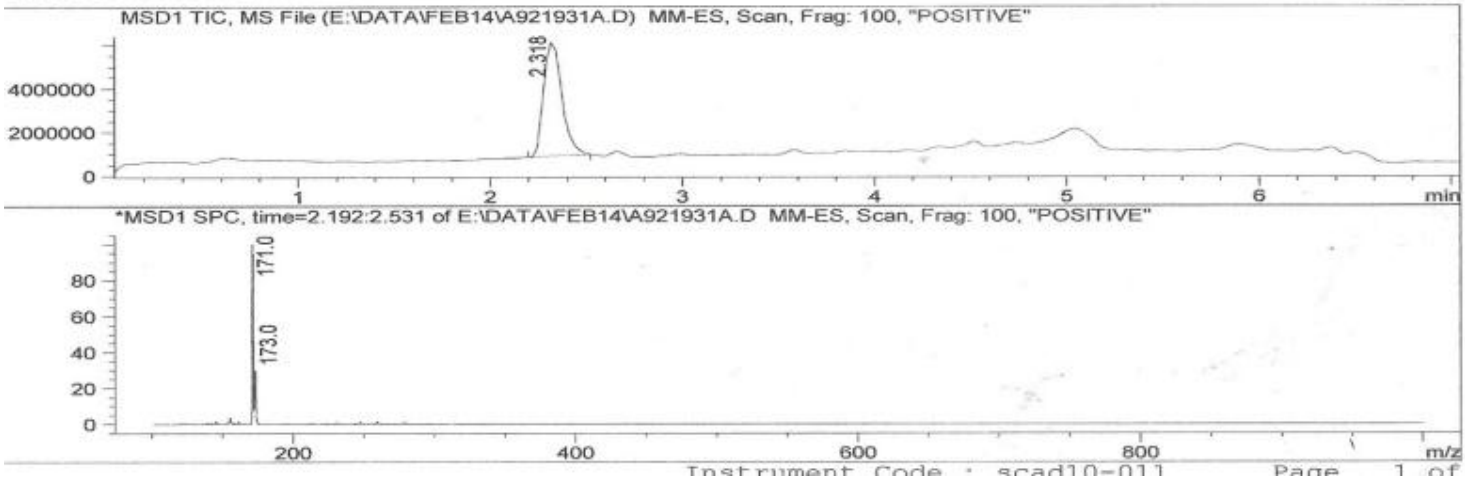



**Figure 10: 1H NMR of compound 1c" in DMSO-$d_6$**

```
ethod info  :A-10mM Ammonium acetate in water;B-Acetonitrile  Flow: 1.2ml/min,
             Column-ZOXBAX  XDB C18 (50X4.6mm-5µm, )  positive& negative
             TIME (MIN)  :  0--3.0     3.0--5.0     5.0--5.5     5.5-7.0
                    %B            10-95        95        95-10          10
```

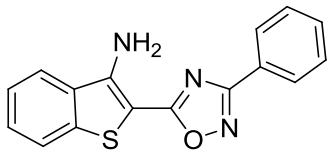



| Peak No | RT min | Area | Area % |
|---|---|---|---|
| 1 | 1.276 | 1.605e+001 | 0.178 |
| 2 | 2.292 | 8.975e+003 | 99.702 |
| 3 | 3.555 | 1.075e+001 | 0.119 |




Instrument Code : scad10-011 Page 1 of

**Figure 11: LC-MS of compound 1c”**




Molecular Weight: 293.34

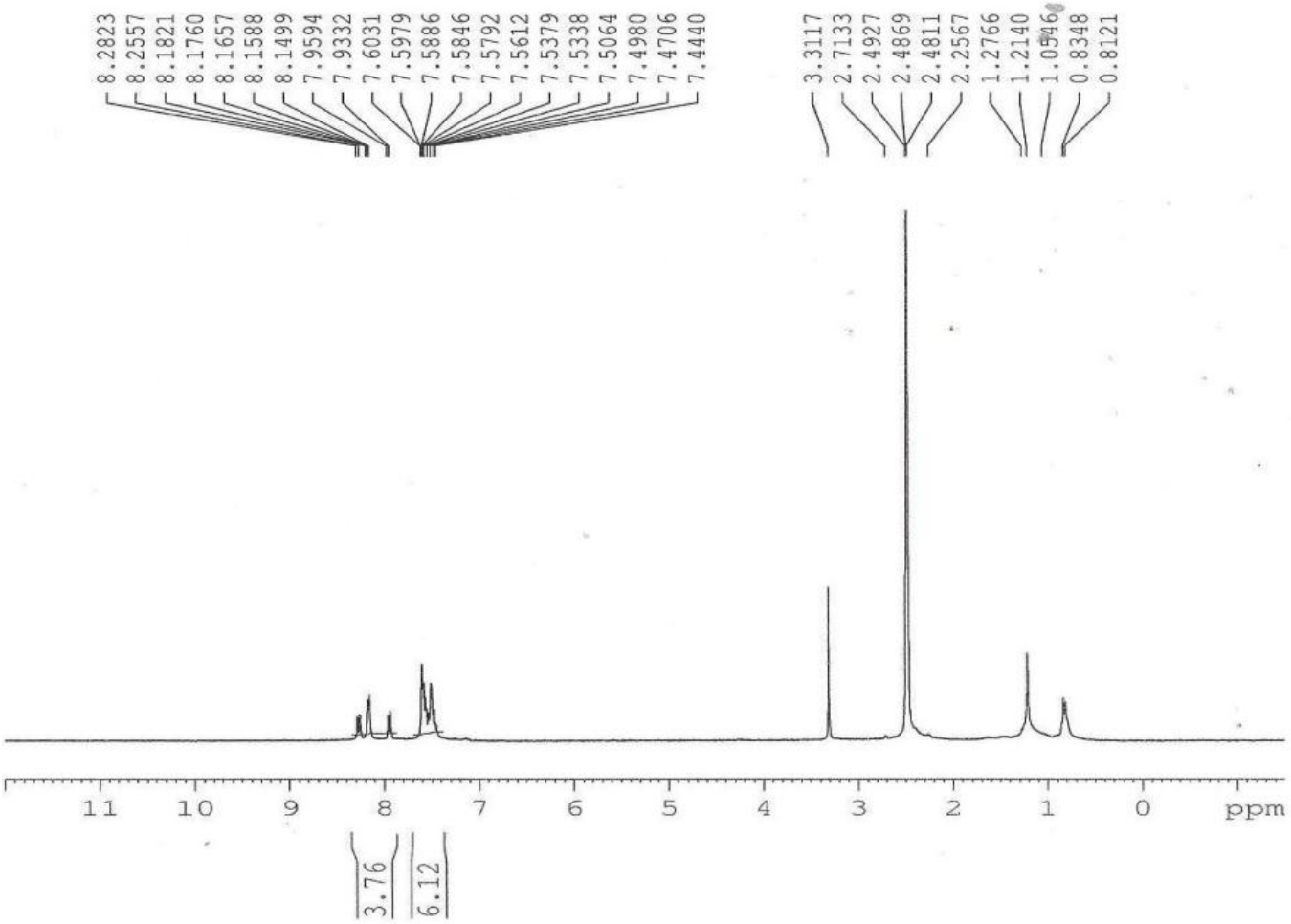



**Figure 12: 1H NMR of compound 2a' in DMSO-$d_6$**

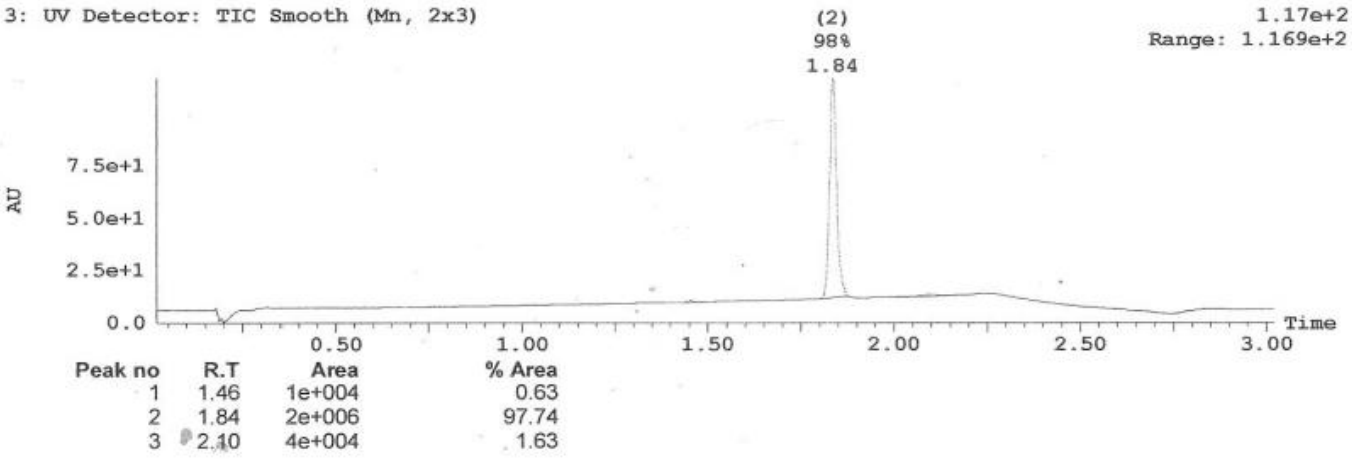
Sample Name:IS10767-090
Data File:A879691
Acq.Method:595FA.olp
Instrument Code :SC\AD\17-004

Mobile A:0.1%HCOOH in Water
Mobile B: 0.1%HCOOH in ACN
%B: 0min=5%2min=95%2.5min=5%3min=5%

Vial:1:15
Flow Rate:1.0 ml/min
Inj Date:03-Jan-2014
Column : Acquity UPLC HSS T3 (2.1x50)mm;1.8µm:

Printed: Fri Jan 03 11:33:26 2014

**Sample Report:**




| Peak no | R.T | Area | % Area |
|---|---|---|---|
| 1 | 1.46 | 1e+004 | 0.63 |
| 2 | 1.84 | 2e+006 | 97.74 |
| 3 | 2.10 | 4e+004 | 1.63 |

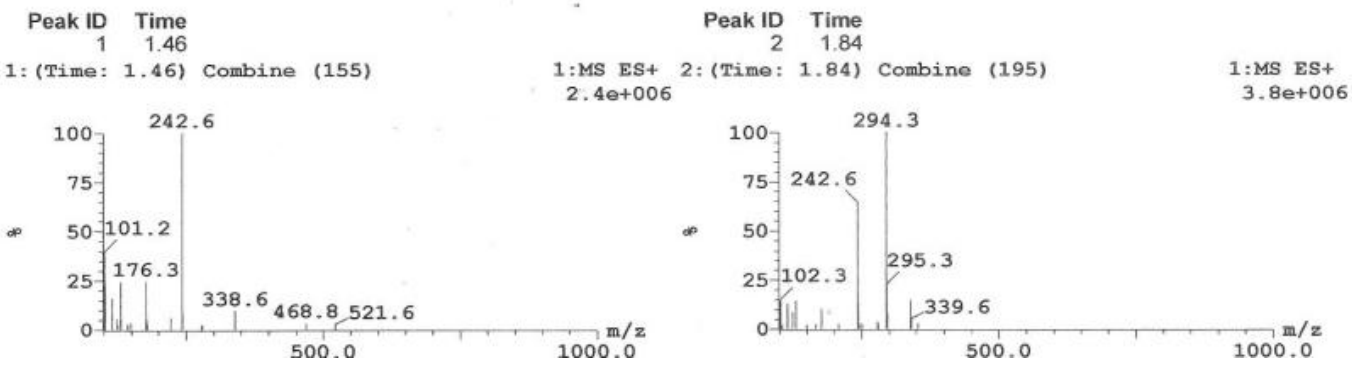
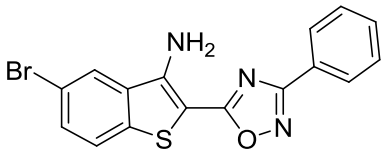



**Figure 13: LC-MS of compound 2a'**




Molecular Weight: 372.24

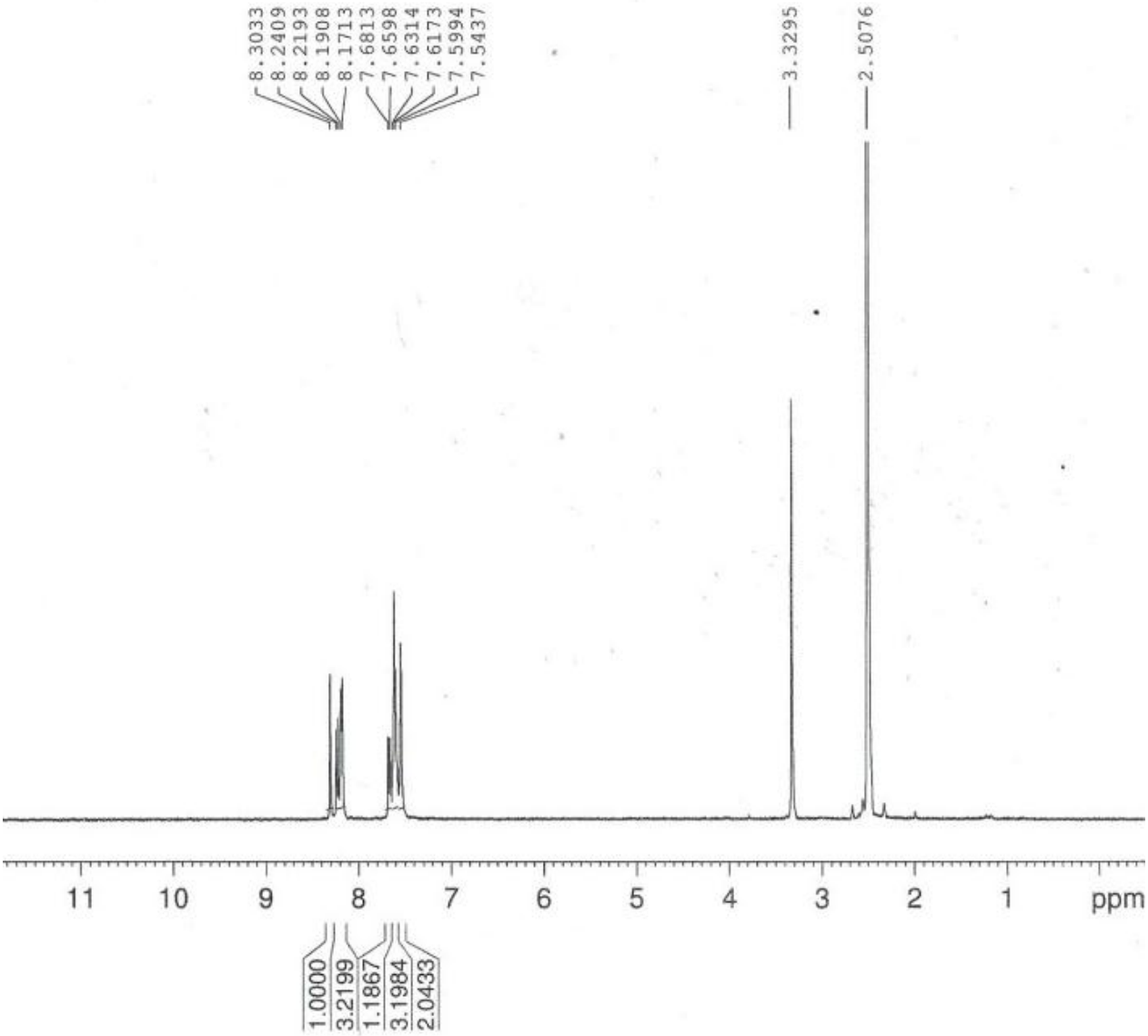



**Figure 14: 1H NMR of compound 2c' in DMSO-$d_6$**

Sample Report:

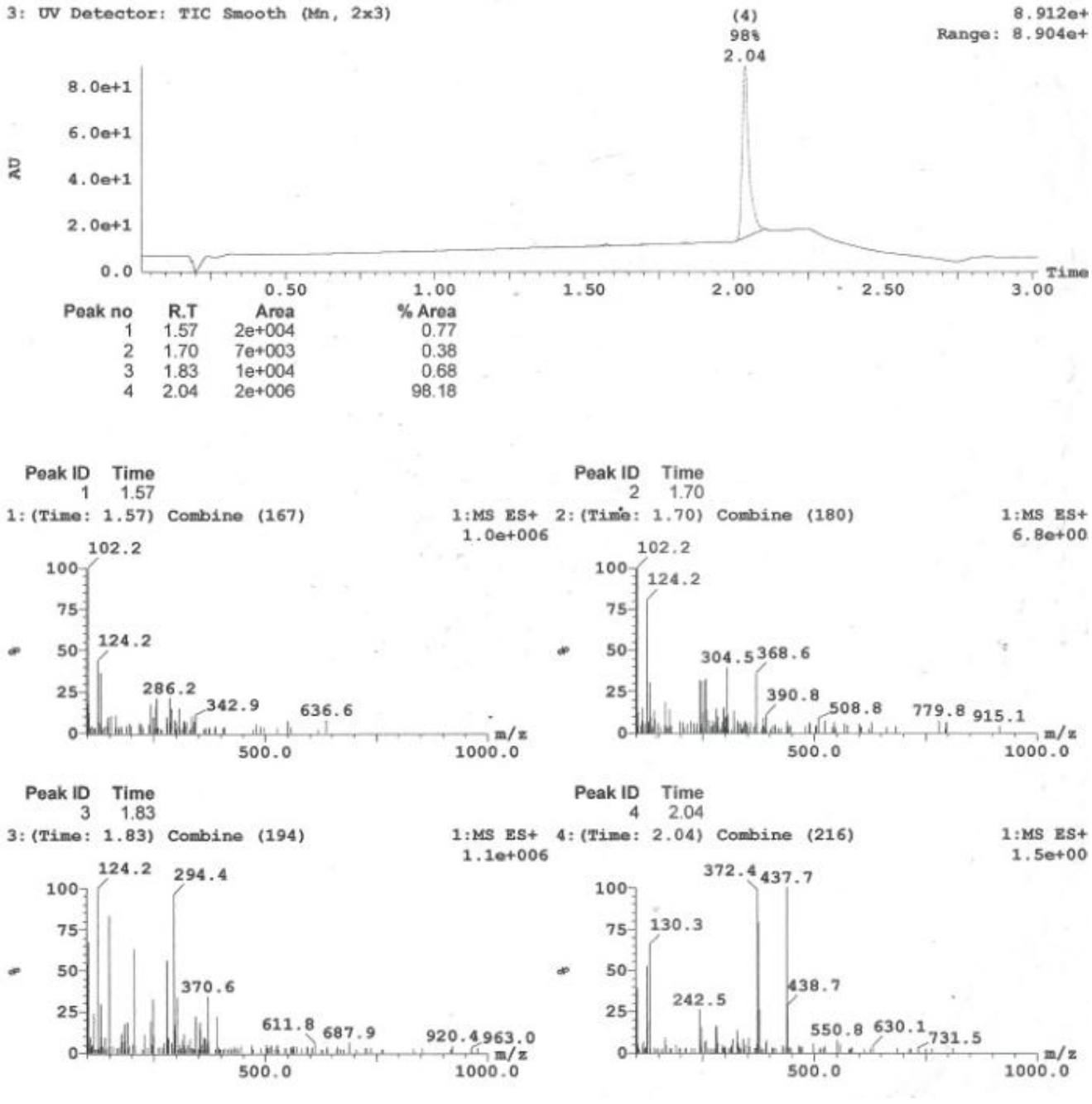
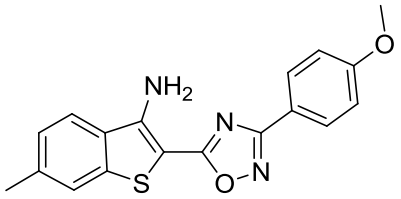



**Figure 15: LC-MS of compound 2c'**




Molecular Weight: 337.40

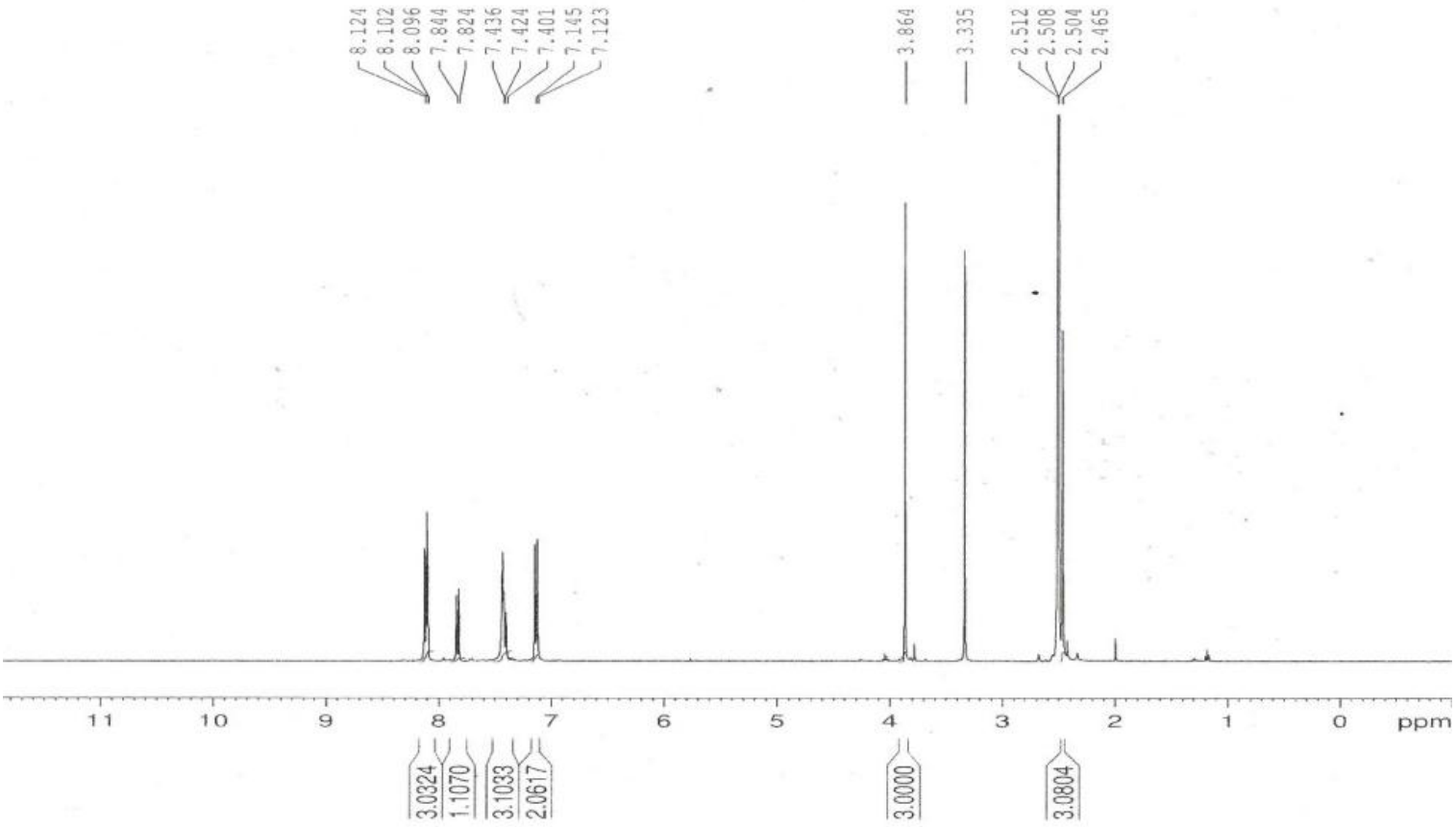
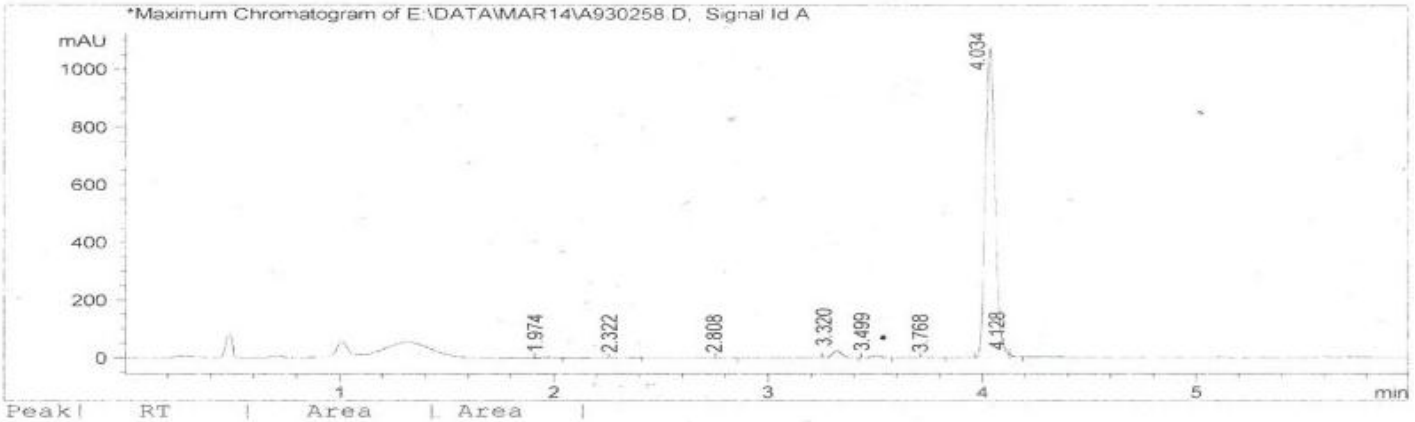


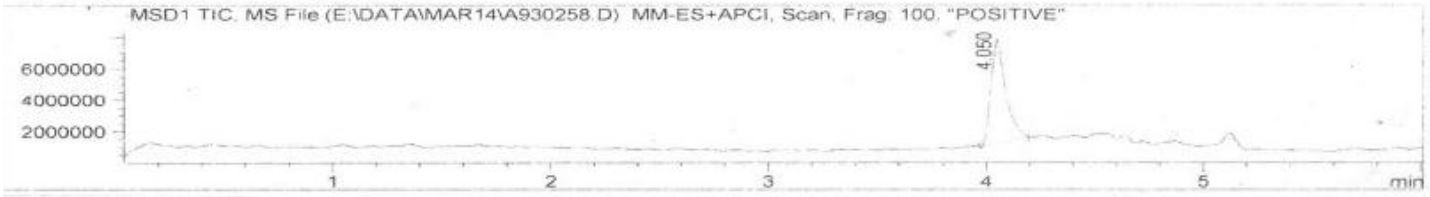

**Figure 16: 1H NMR of compound 2g' in DMSO-$d_6$**

Method info :A-0.1%HCOOH;B-ACN Flow: 1.5ml/min,
Column-Atlantis dC18 (50X4.6mm-5µm, ) positive mode & Negative mode

| TIME (MIN) | 0--3.0 | 3.0--4.0 | 4.0--4.5 | 4.5-6.0 |
|---|---|---|---|---|
| %B | 5-95 | 95 | 95-5 | 5 |




| Peak No | RT min | Area | Area % |
|---|---|---|---|
| 1 | 1.974 | 9.748e+000 | 0.282 |
| 2 | 2.322 | 4.046e+000 | 0.117 |
| 3 | 2.808 | 1.725e+000 | 0.050 |
| 4 | 3.320 | 7.230e+001 | 2.089 |
| 5 | 3.499 | 2.427e+001 | 0.701 |
| 6 | 3.768 | 4.408e+000 | 0.127 |
| 7 | 4.034 | 3.337e+003 | 96.400 |
| 8 | 4.128 | 8.120e+000 | 0.235 |



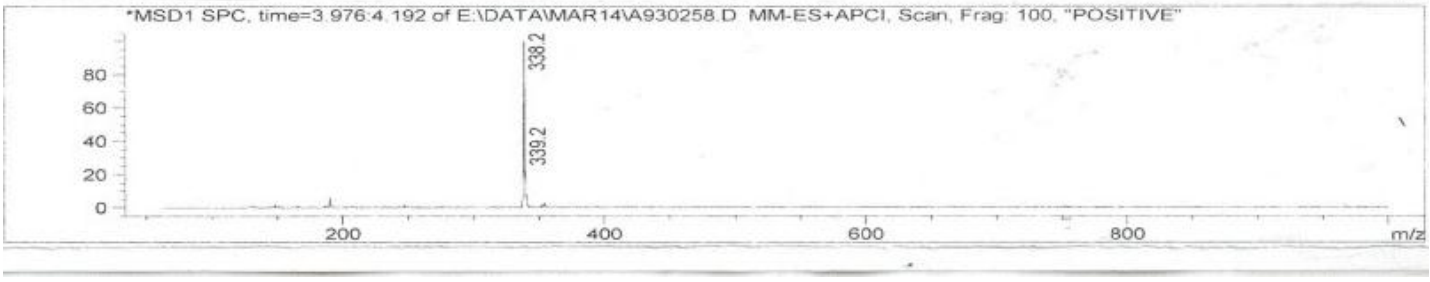
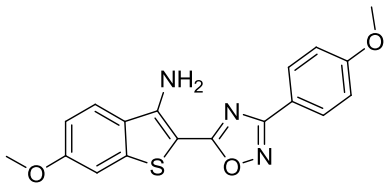




**Figure 17: LC-MS of compound 2g'**




Molecular Weight: 353.39

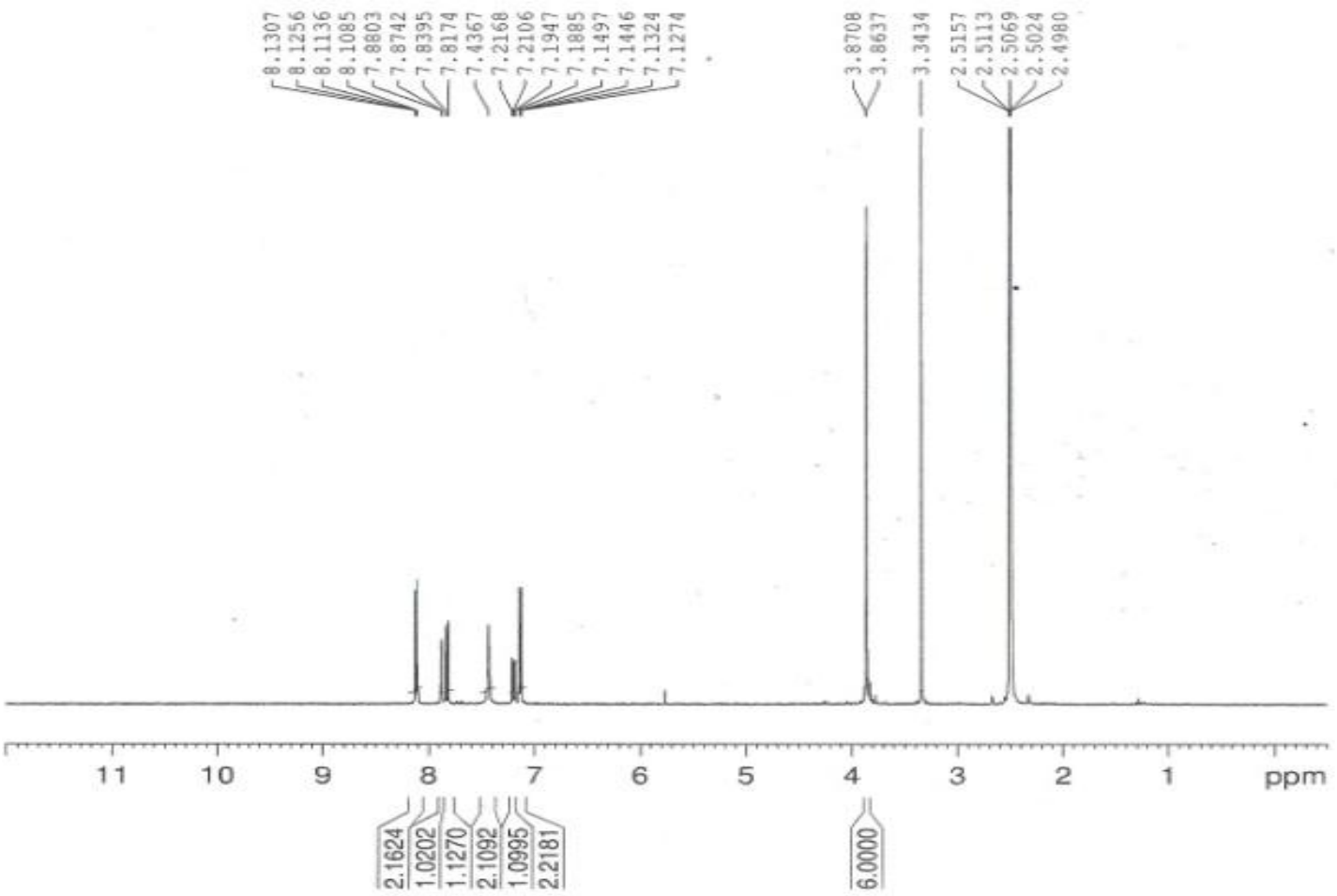
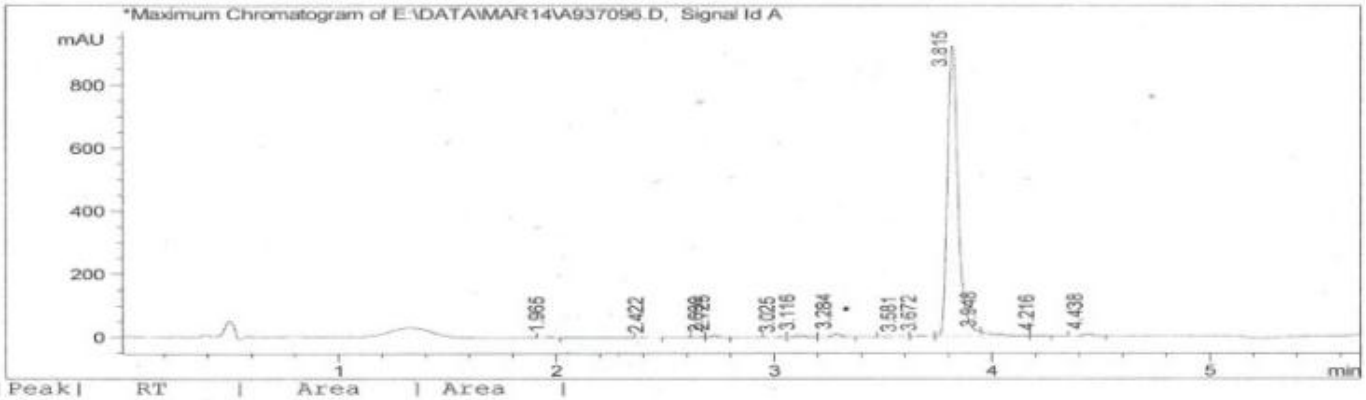



**Figure 18: 1H NMR of compound 2i' in DMSO-$d_6$**




| Peak No | RT min | Area | Area % |
|---|---|---|---|
| 1 | 1.965 | 1.192e+001 | 0.353 |
| 2 | 2.422 | 5.622e+000 | 0.167 |
| 3 | 2.699 | 8.198e+000 | 0.243 |
| 4 | 2.725 | 2.270e+001 | 0.673 |
| 5 | 3.025 | 5.448e+000 | 0.162 |
| 6 | 3.116 | 2.474e+001 | 0.733 |
| 7 | 3.284 | 3.643e+001 | 1.080 |
| 8 | 3.581 | 4.644e+000 | 0.138 |
| 9 | 3.672 | 1.088e+001 | 0.323 |
| 10 | 3.815 | 3.148e+003 | 93.335 |
| 11 | 3.948 | 6.363e+001 | 1.886 |
| 12 | 4.216 | 7.537e+000 | 0.223 |
| 13 | 4.438 | 2.306e+001 | 0.684 |

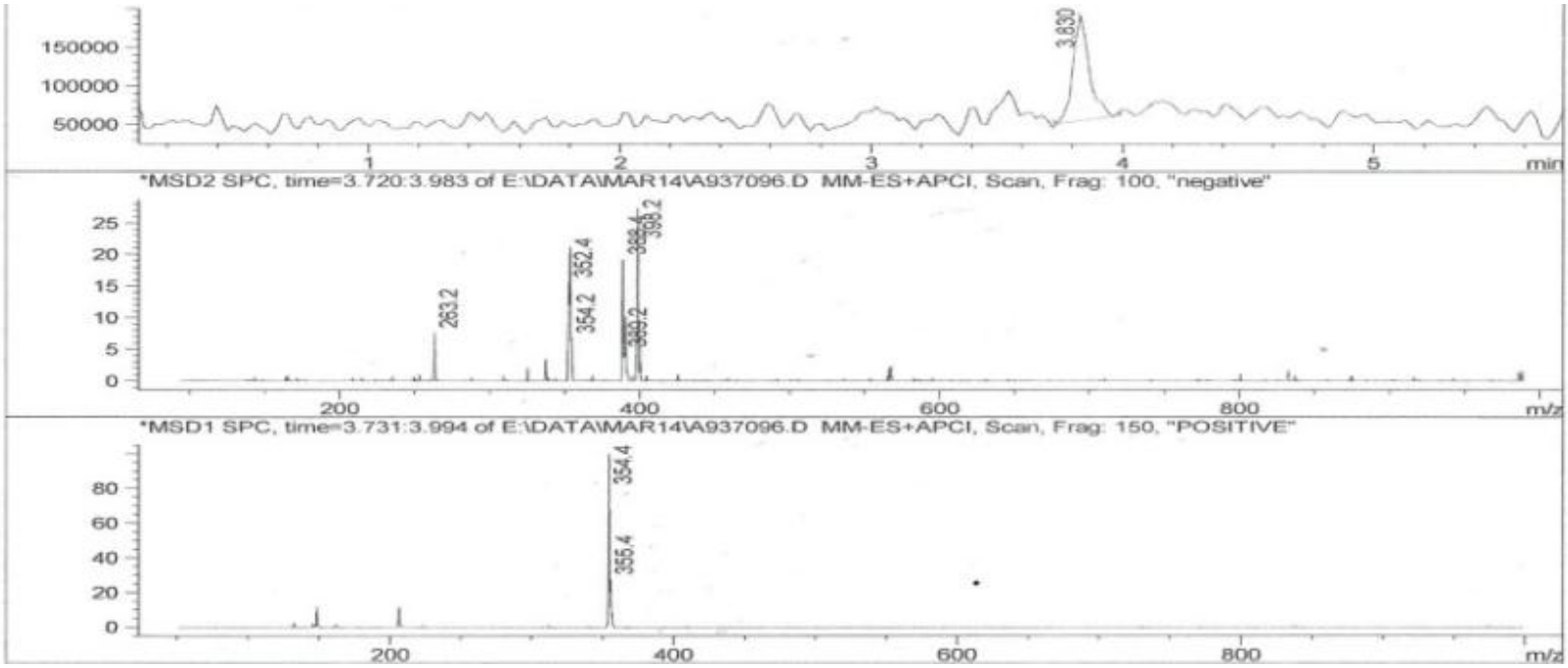
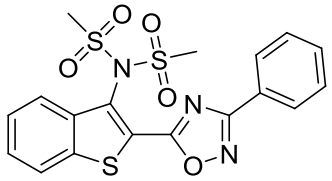



**Figure 19: LC-MS of compound 2i'**



Molecular Weight: 449.52

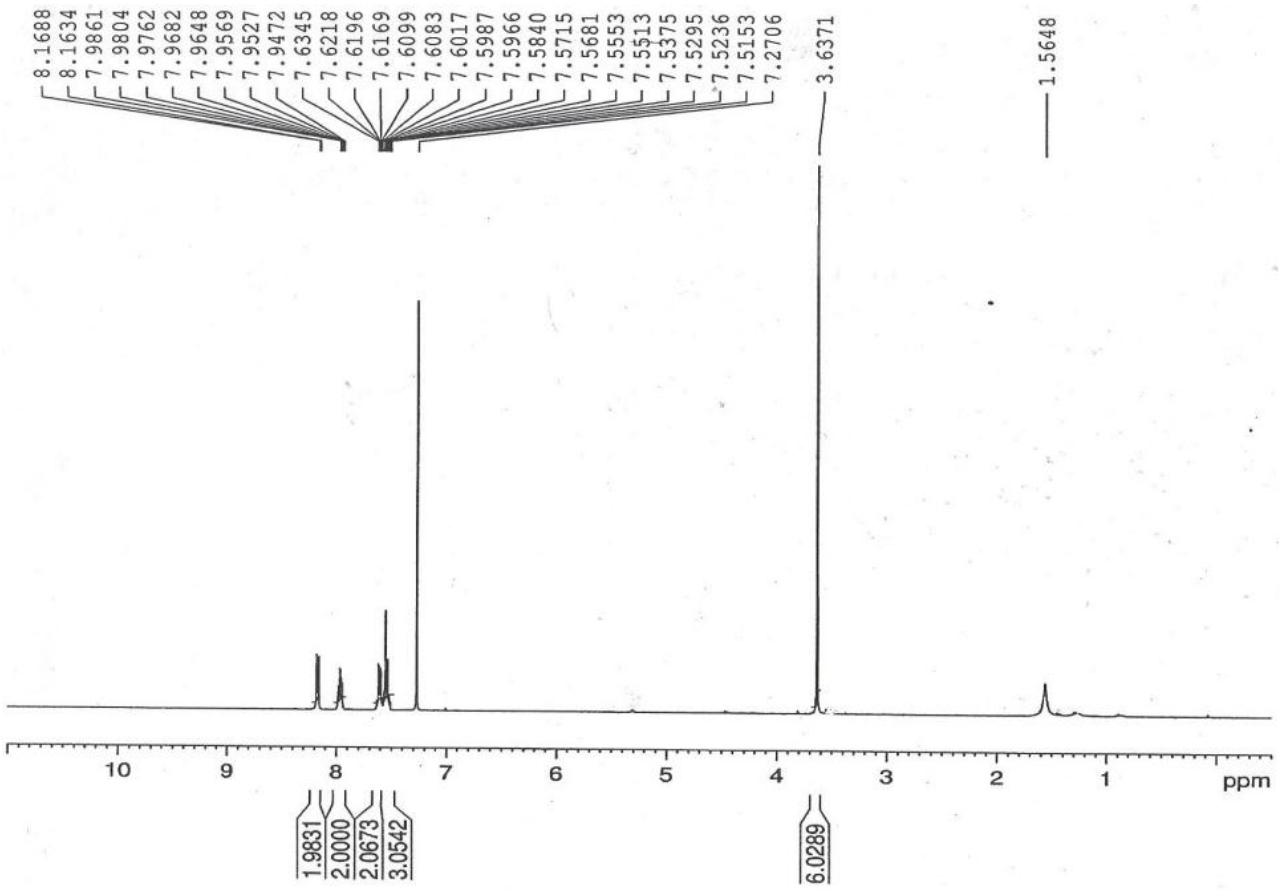



**Figure 20: $^{1}$H NMR of compound 3a in $CDCl_3$**

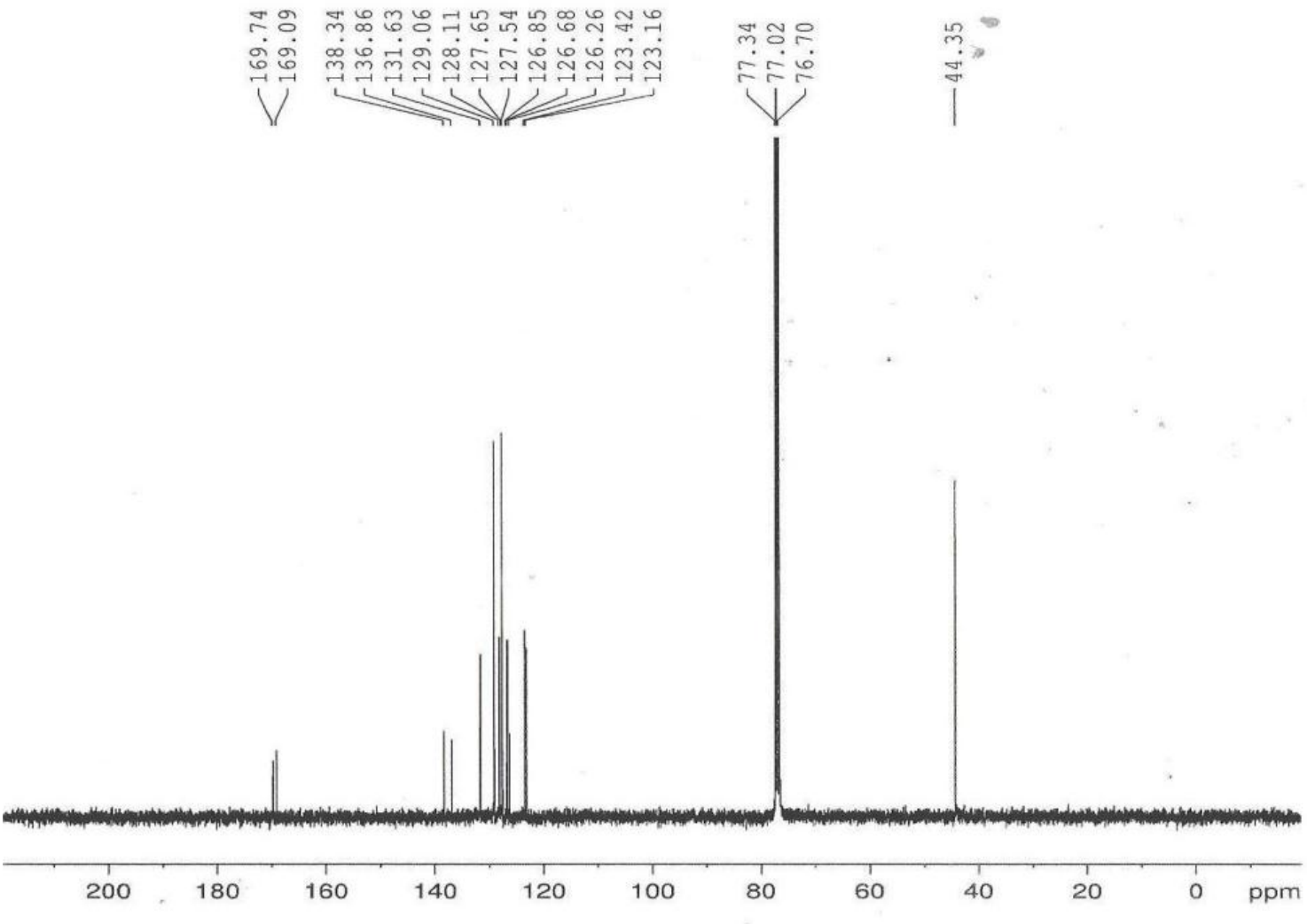
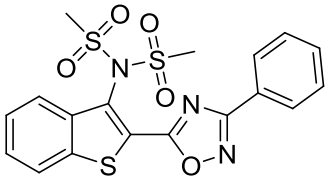



**Figure 21: $^{13}C$ NMR of compound 3a in $CDCl_3$**



Molecular Weight: 449.52

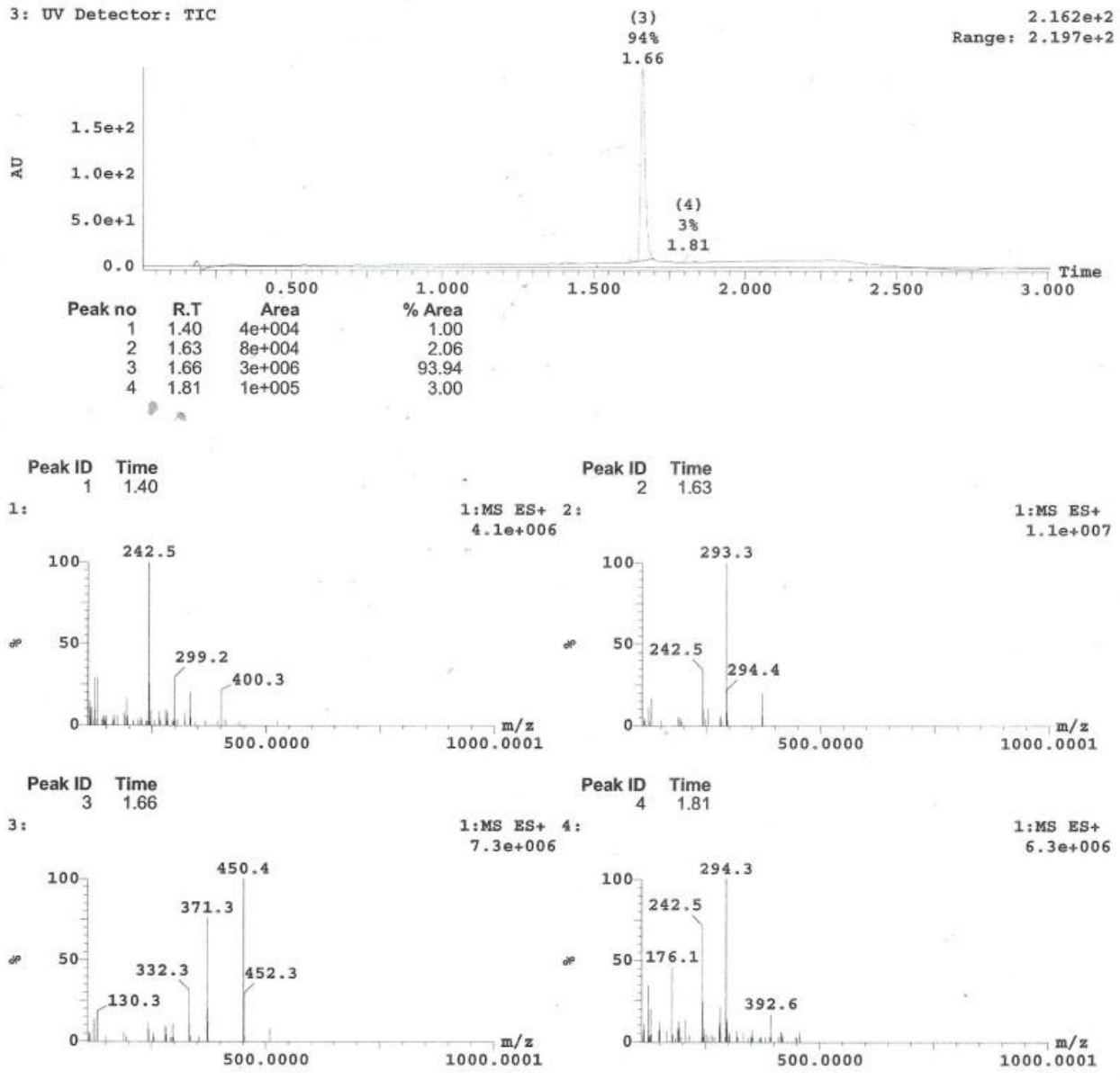



**Figure 22: LC-MS of compound 3a**

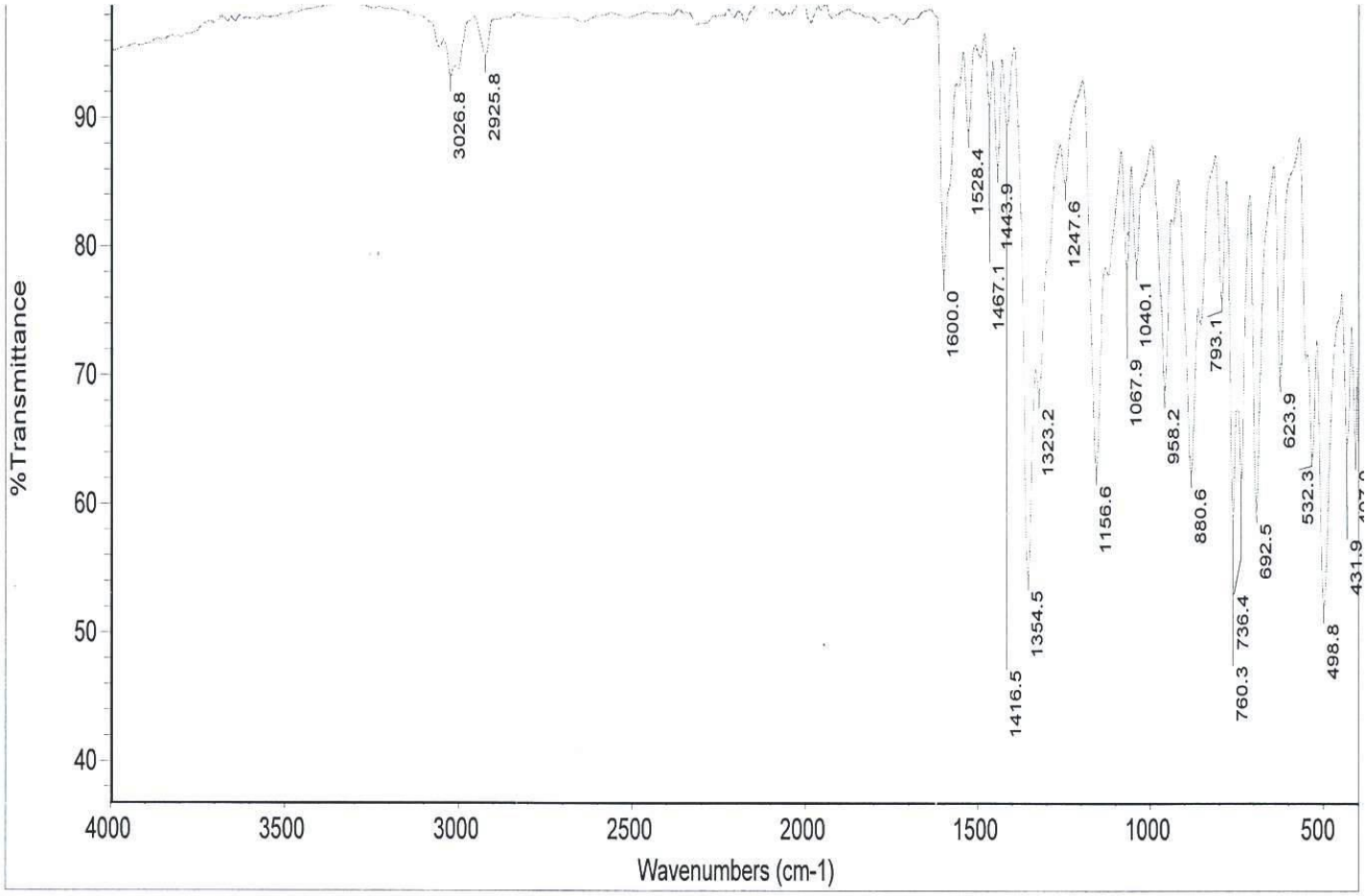
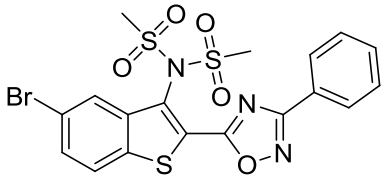



**Figure 23: IR spectra of compound 3[a]**




Molecular Weight: 528.42

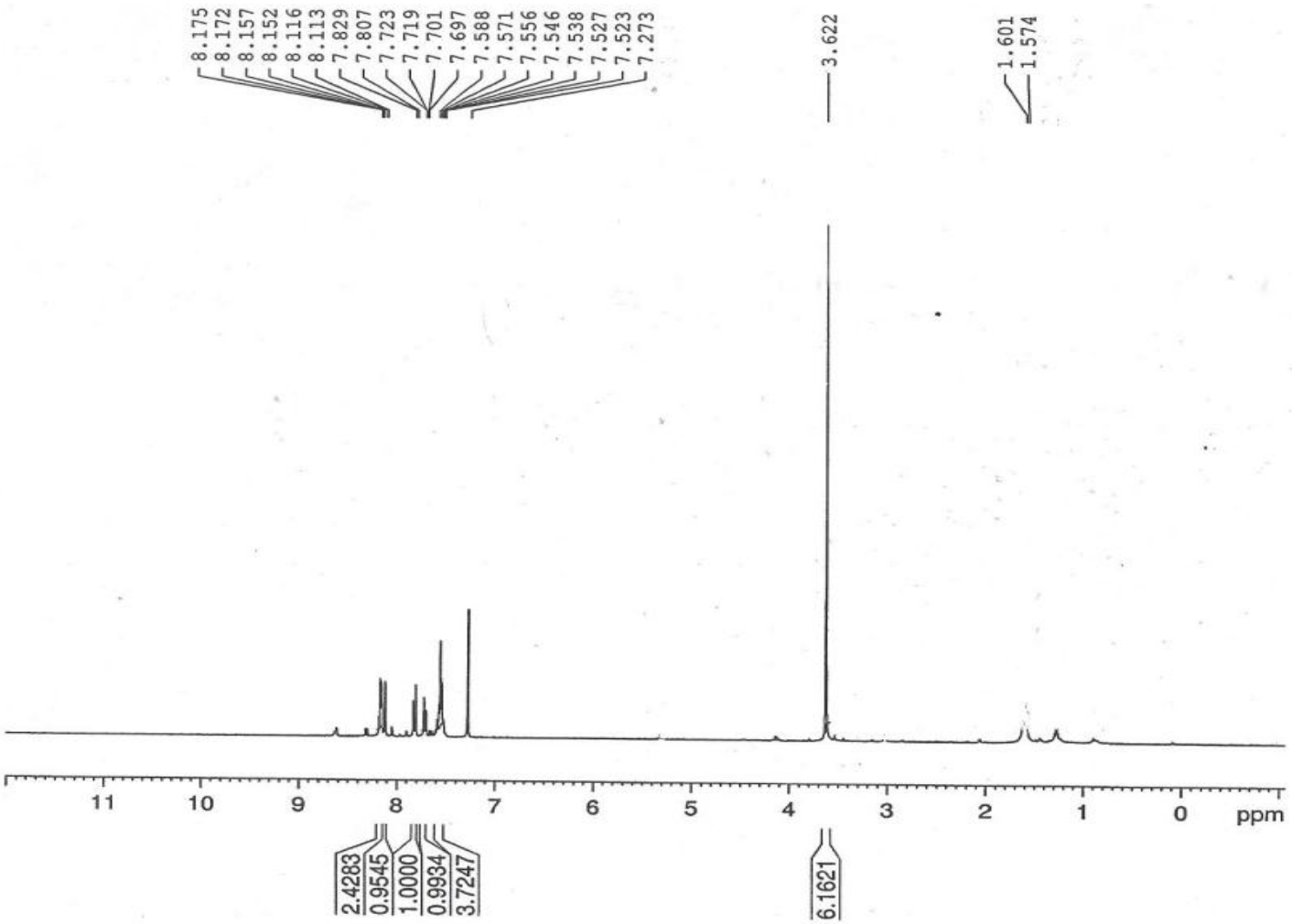



**Figure 24: $^{1}$H NMR of compound 3c in $CDCl_3$**

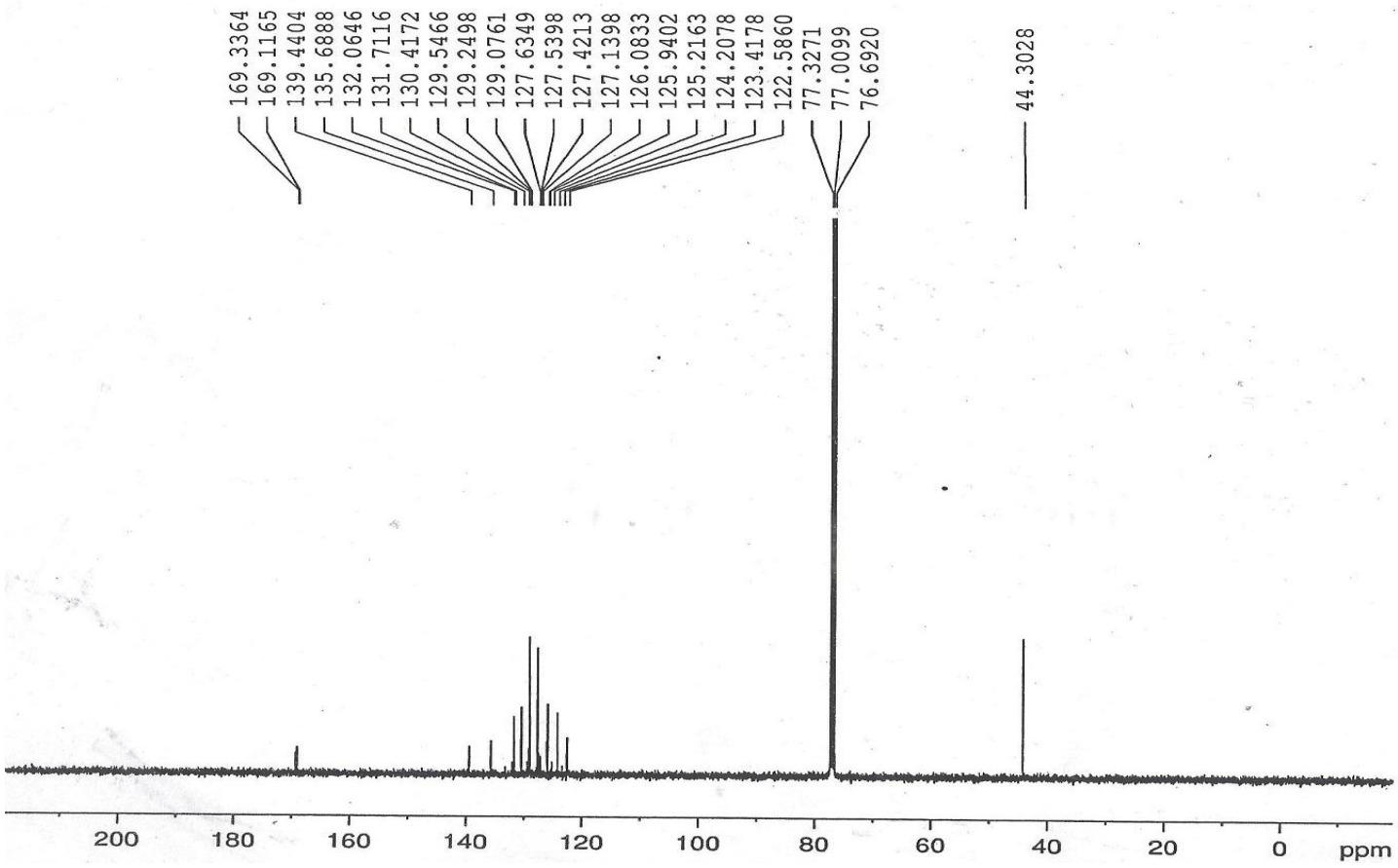
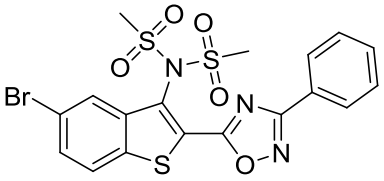



**Figure 25: $^{13}C$ NMR of compound 3c in $CDCl_3$**




Molecular Weight: 528.42

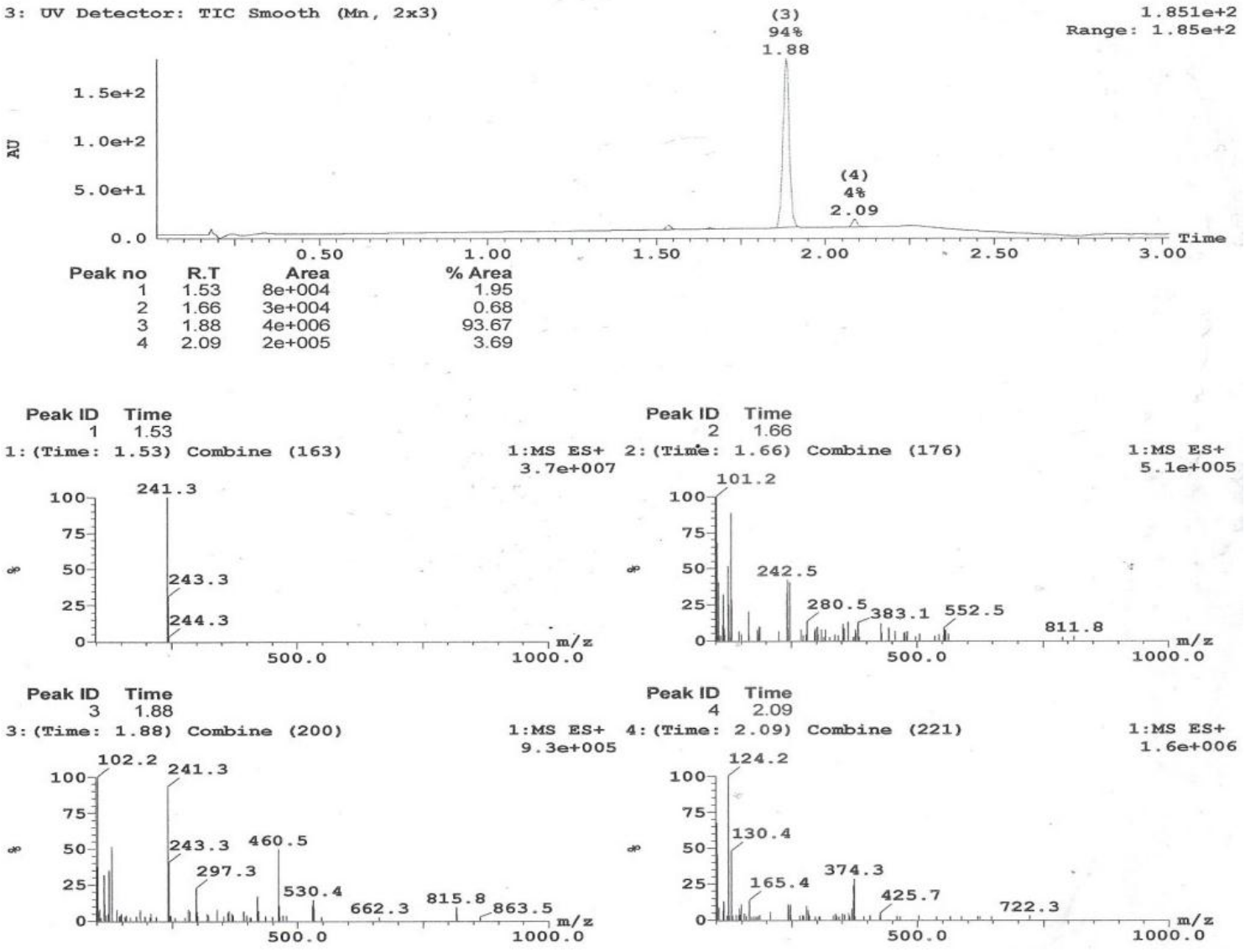



**Figure 26: LC-MS of compound 3c**

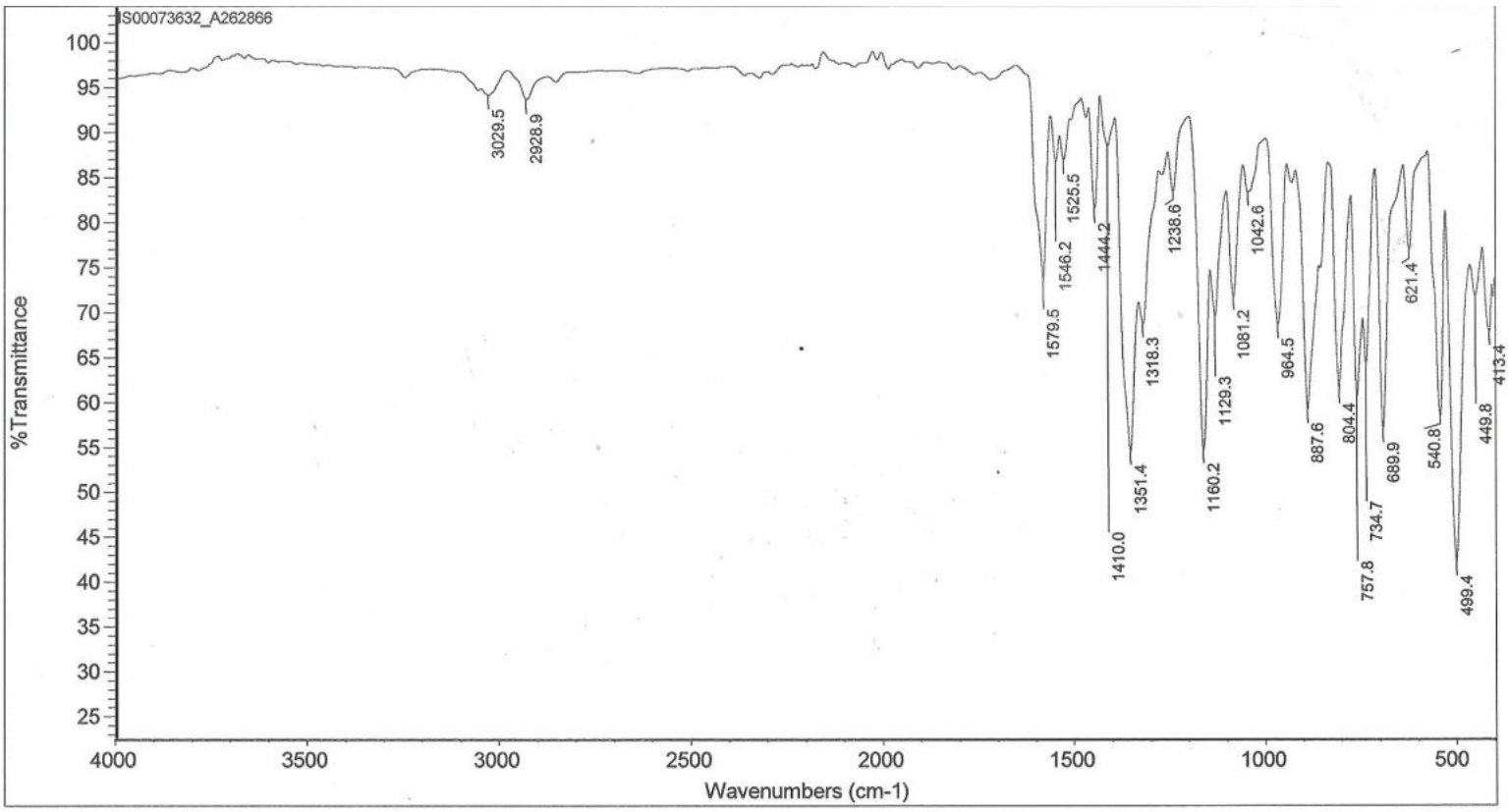



**Figure 27: IR spectra of compound 3c**

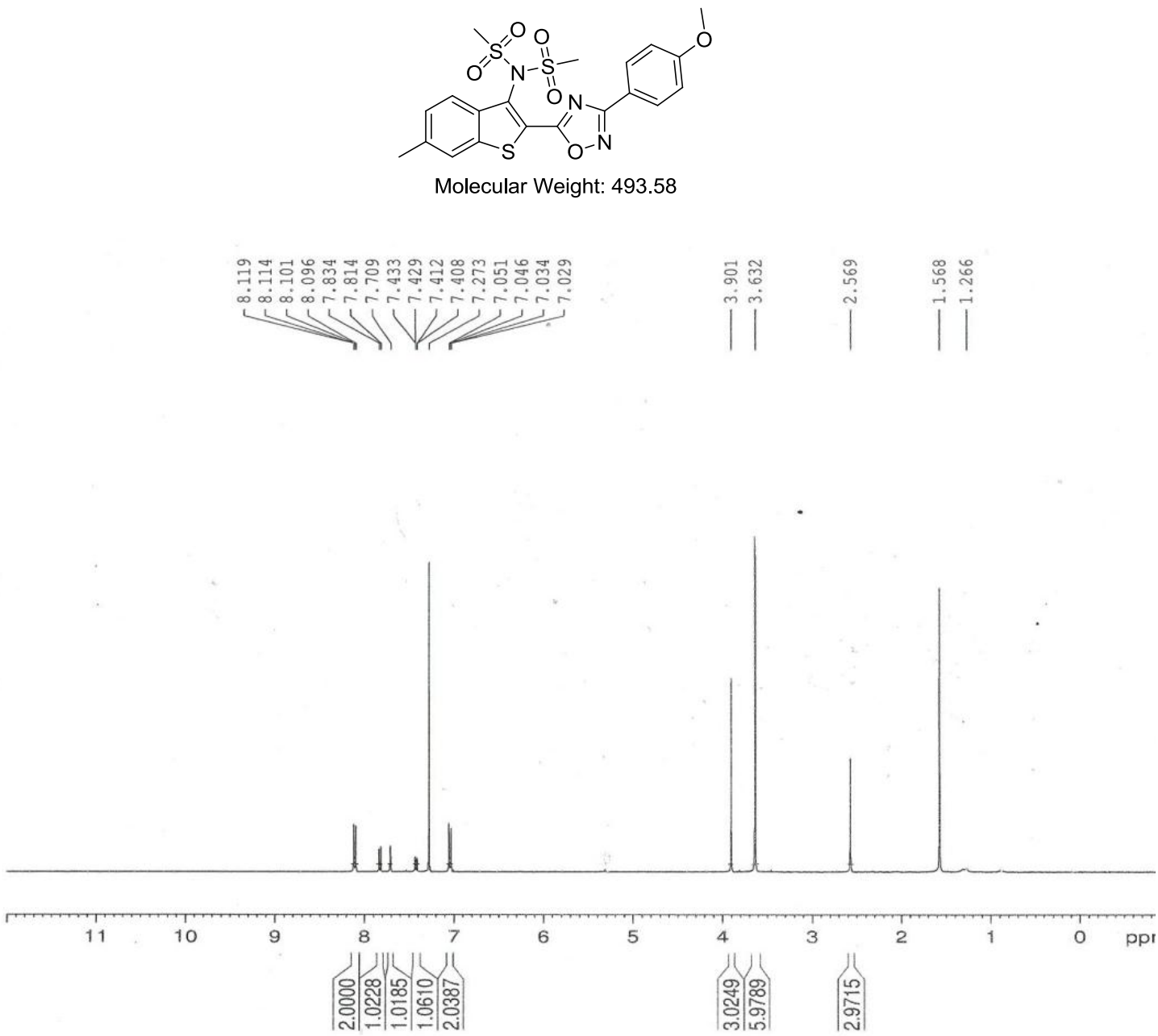



**Figure 28: $^{1}$H NMR of compound 3h in $CDCl_3$**

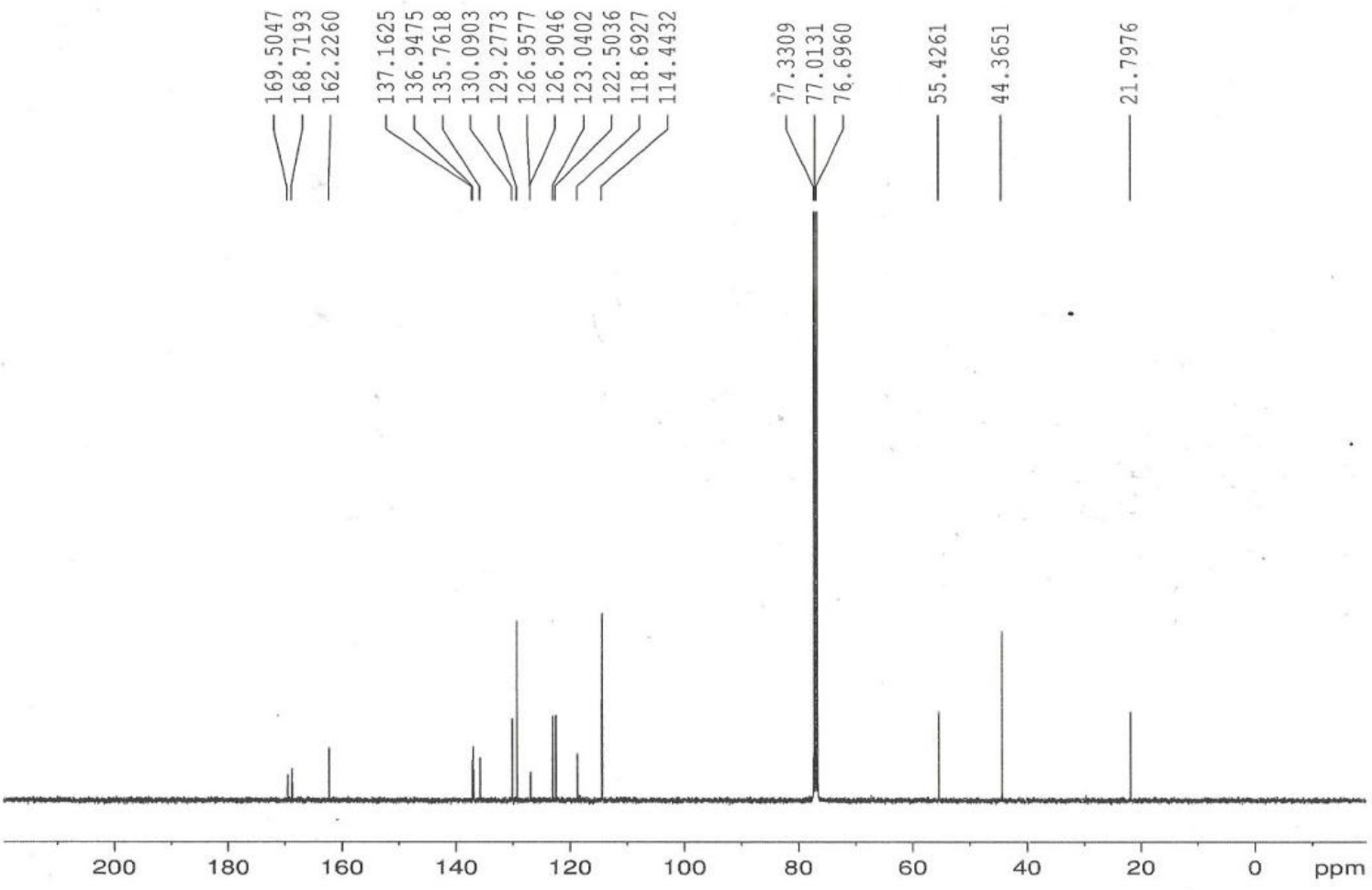
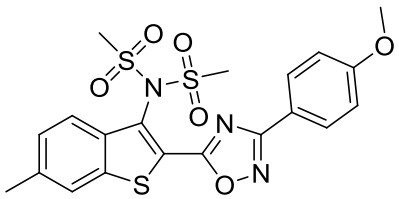
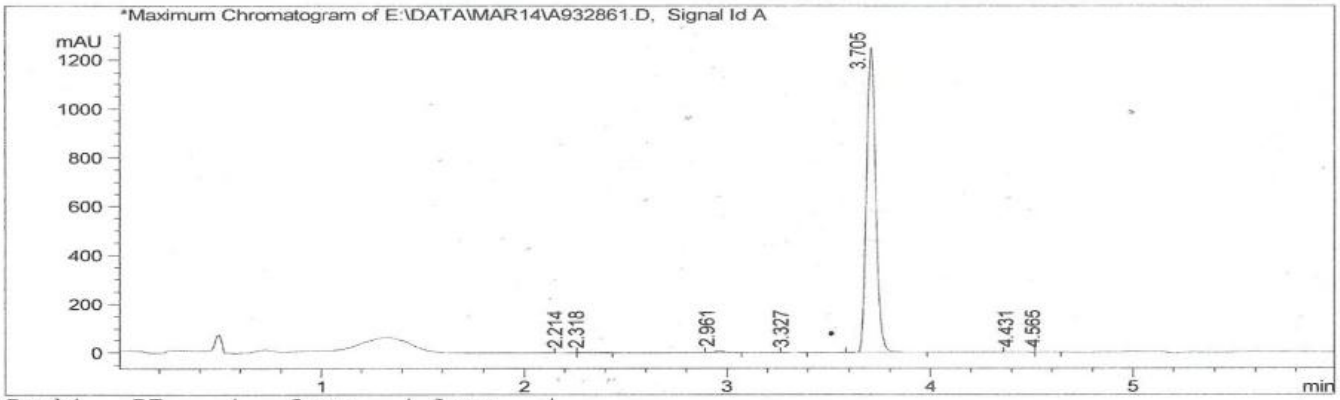



**Figure 29: $^{13}C$ NMR of compound 3h in $CDCl_3$**



Molecular Weight: 493.58

```
Method info   :A-0.1%HCOOH;B-ACN   Flow: 1.5ml/min,
               Column-Atlantis dC18 (50X4.6mm-5µm, )   positive mode & Negative mode
               TIME (MIN)   :   0--3.0      3.0--4.0      4.0--4.5      4.5-6.0
                     %B          5-95          95          95-5            5
```




| Peak No | RT min | Area | Area % |
|---|---|---|---|
| 1 | 2.214 | 1.403e+000 | 0.035 |
| 2 | 2.318 | 5.779e+000 | 0.146 |
| 3 | 2.961 | 1.949e+001 | 0.491 |
| 4 | 3.327 | 3.691e+000 | 0.093 |
| 5 | 3.705 | 3.932e+003 | 99.122 |
| 6 | 4.431 | 3.077e+000 | 0.078 |
| 7 | 4.565 | 1.397e+000 | 0.035 |

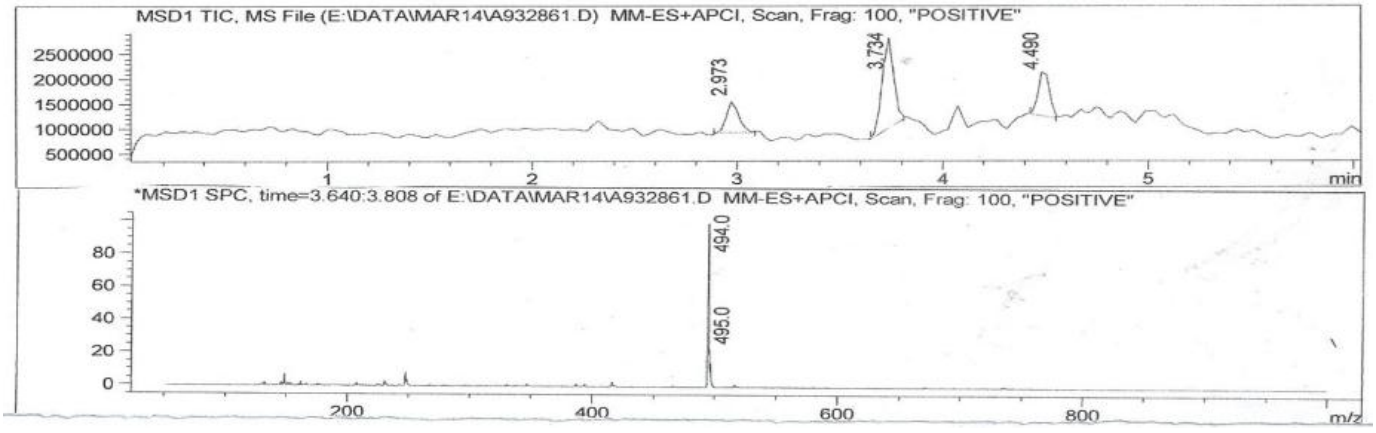



**Figure 30: LC-MS of compound 3h**

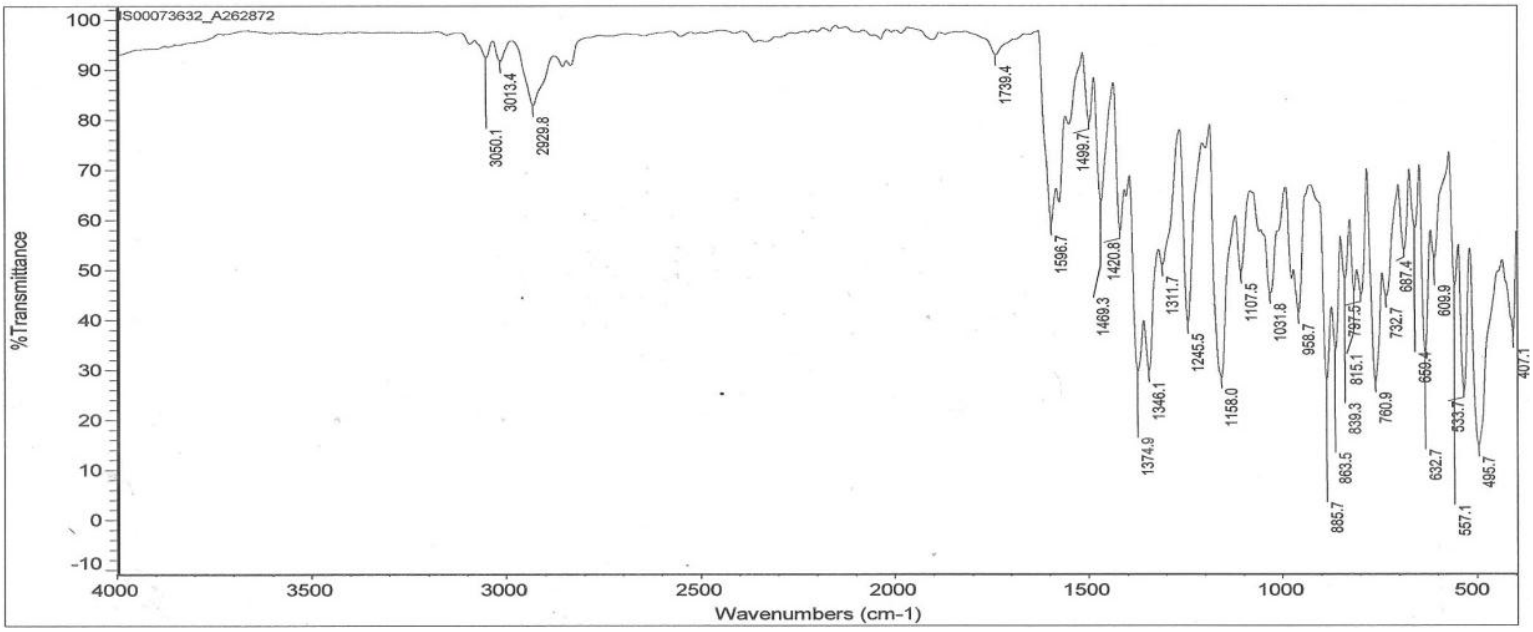
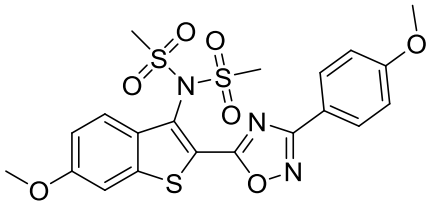



**Figure 31: IR spectra of compound 3h**



Molecular Weight: 509.58

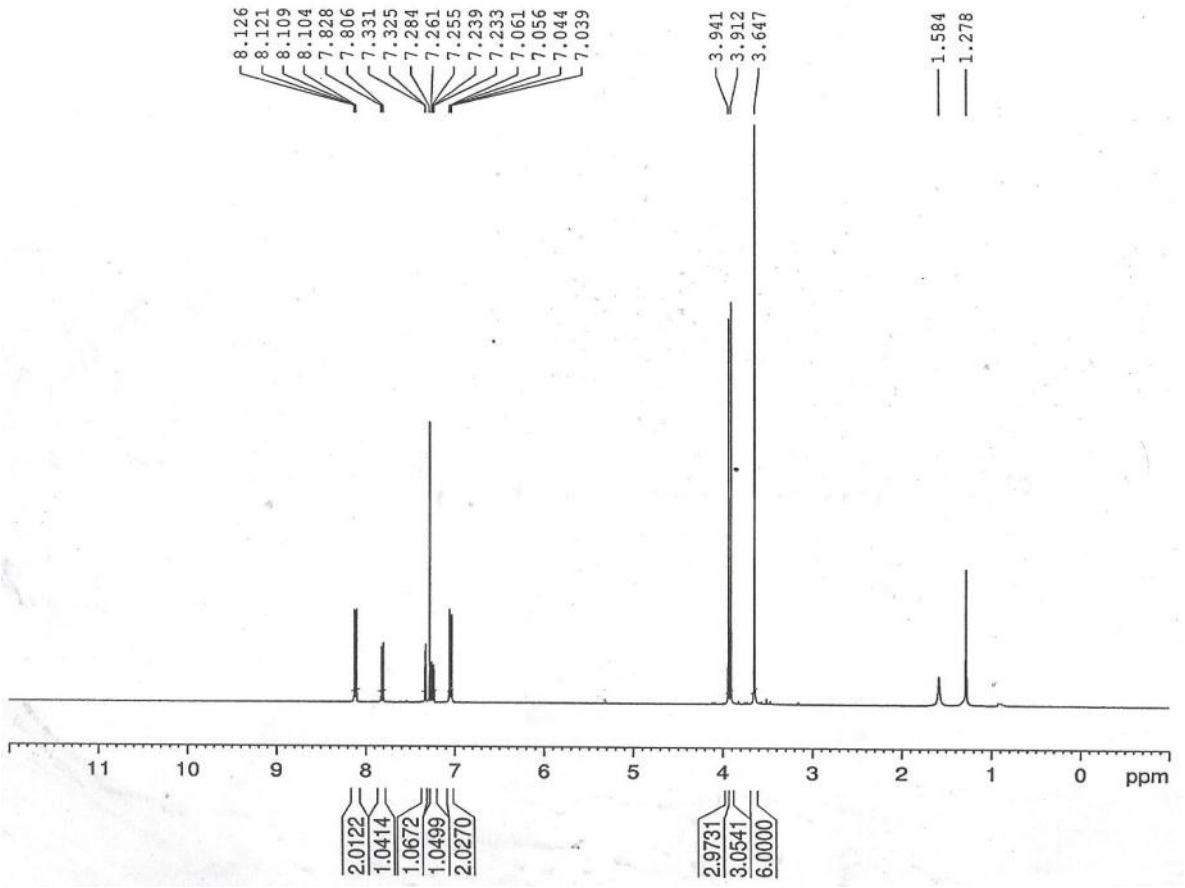



**Figure 32: $^{1}$H NMR of compound 3j in $CDCl_3$**

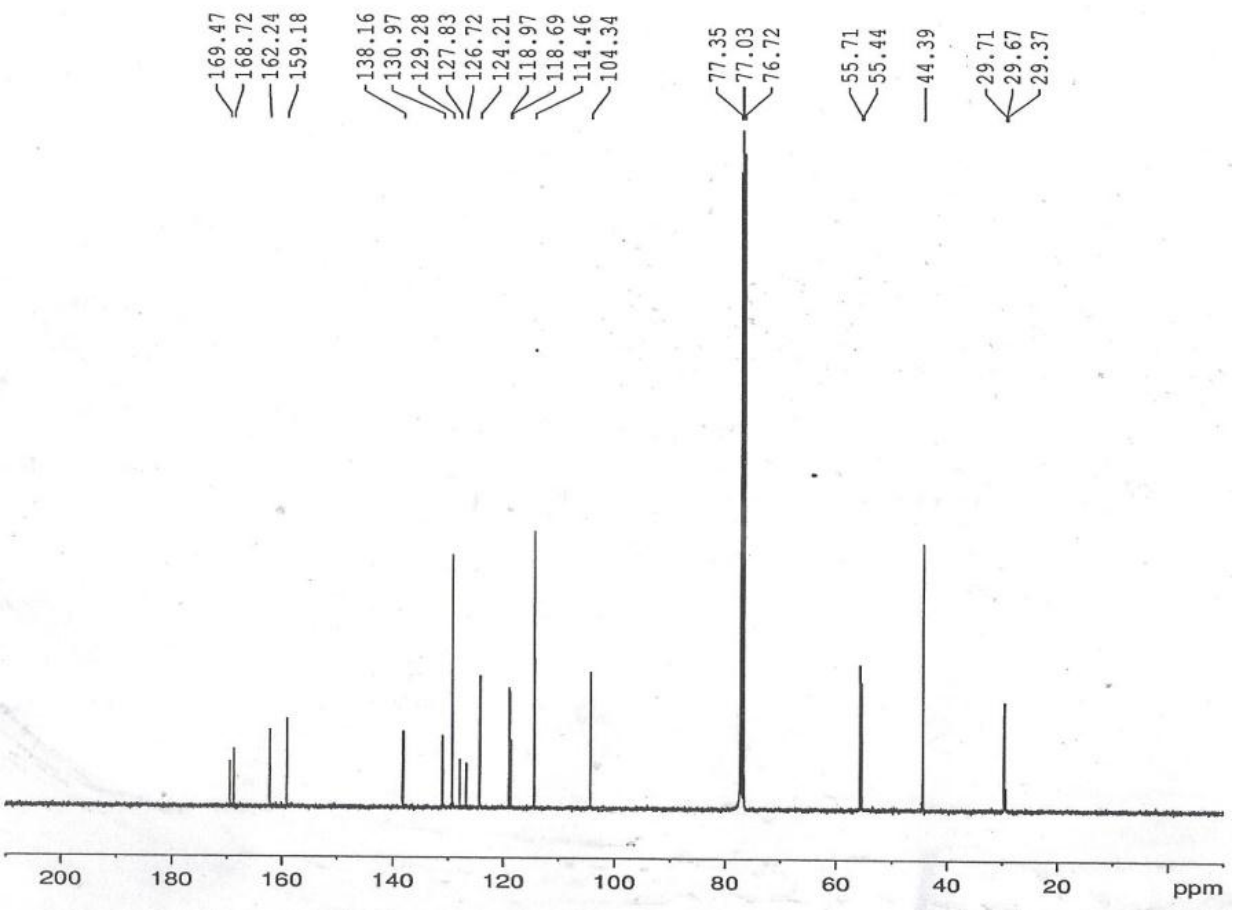
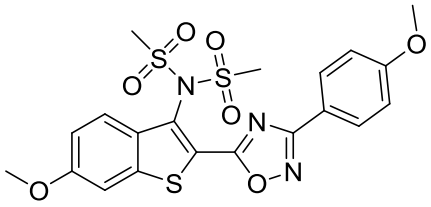
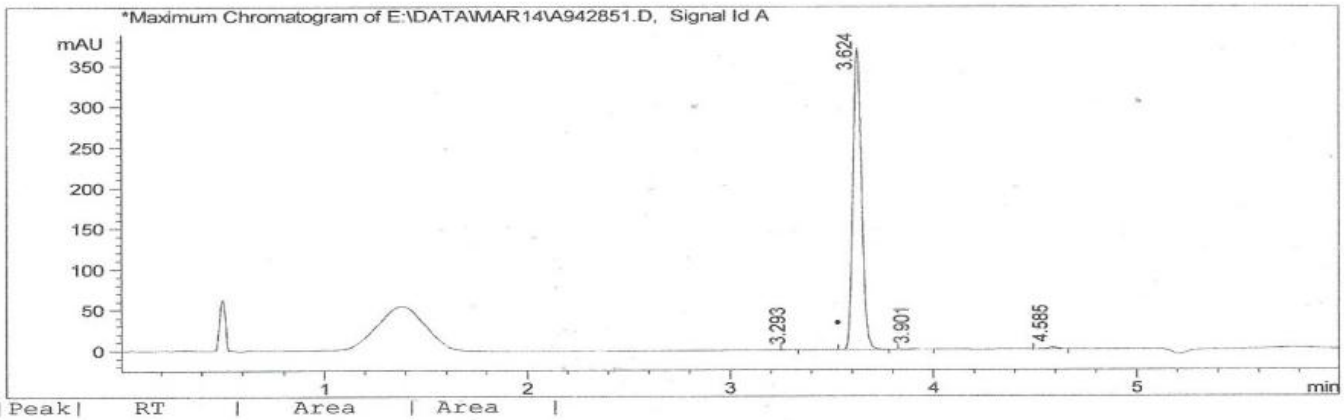



**Figure 33: $^{13}$C NMR of compound 3j in $CDCl_3$**



Molecular Weight: 509.58

```
Method info   :A-0.1%HCOOH;B-ACN   Flow: 1.5ml/min,
               Column-Atlantis dC18 (50X4.6mm-5µm, )   positive mode & Negative mode
               TIME (MIN)   :   0--3.0      3.0--4.0      4.0--4.5      4.5-6.0
                     %B          5-95          95          95-5           5
```




| Peak No | RT min | Area | Area % |
|---|---|---|---|
| 1 | 3.293 | 1.291e+000 | 0.115 |
| 2 | 3.624 | 1.110e+003 | 98.952 |
| 3 | 3.901 | 2.600e+000 | 0.232 |
| 4 | 4.585 | 7.869e+000 | 0.701 |

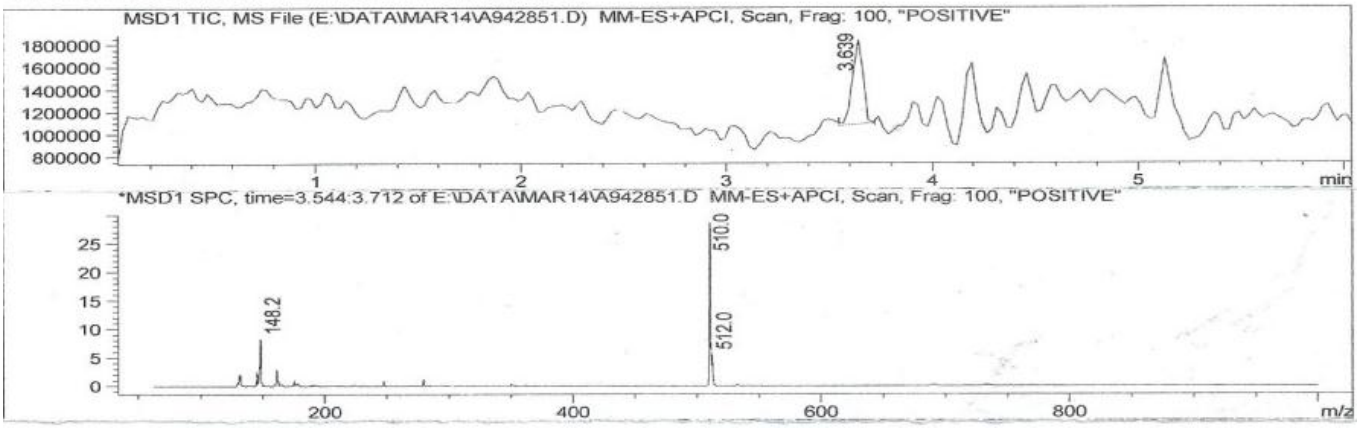



**Figure 34: LC-MS of compound 3j**

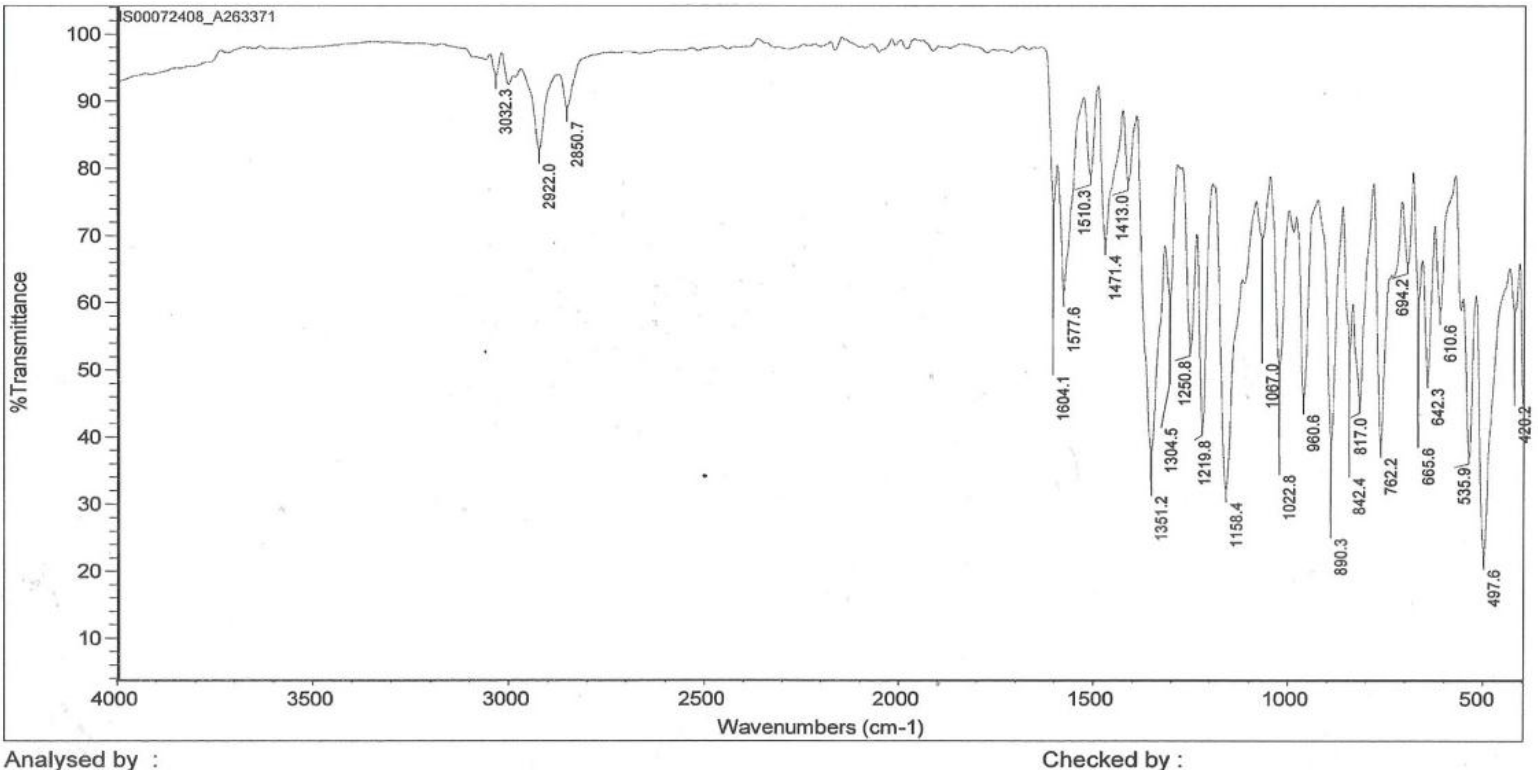
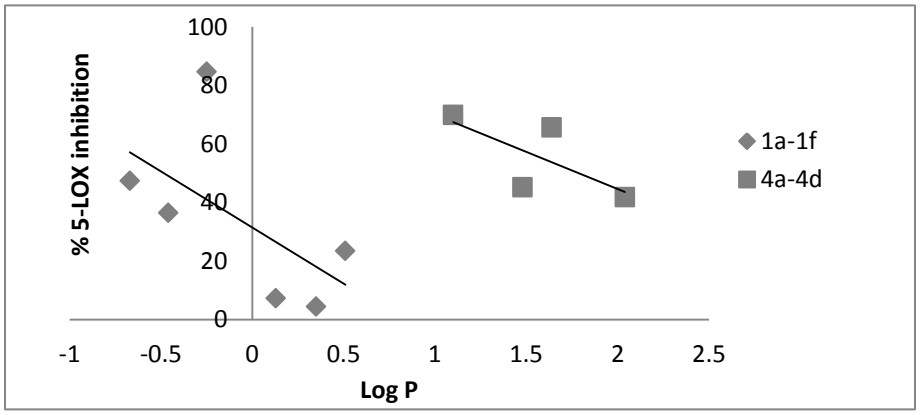


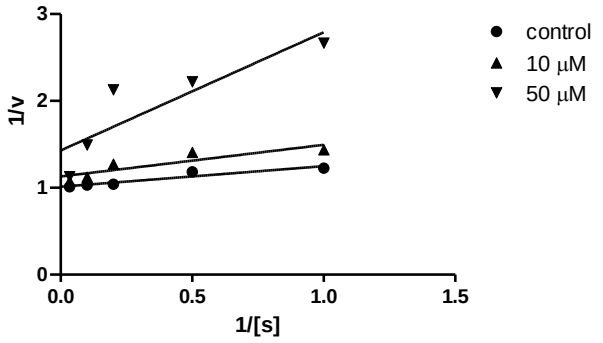

**Figure 35: IR spectra of compound 3j**

**2. Graph between log P and % 5-LOX inhibition for compounds (1a-1f) and (4a-4d).**

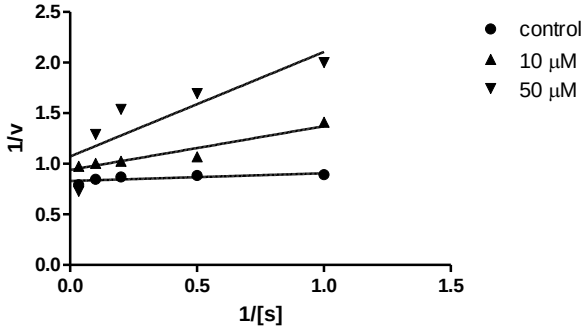



**3. Graphs showing lineweaver-Burk plot for compound 1d and 4a.**

**(Compound 1d)**




**(Compound 4a)**




**(Note : S = Substrate, Arachidonic acid ; V = velocity of the reaction)**